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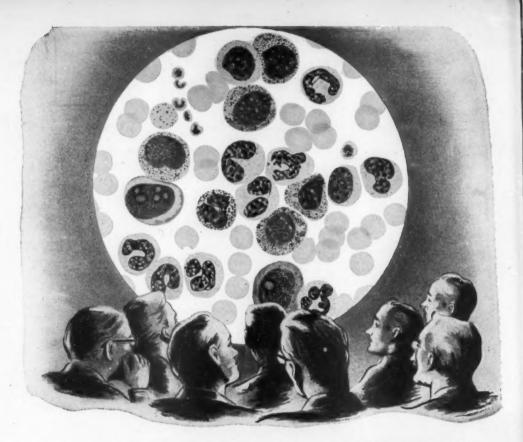
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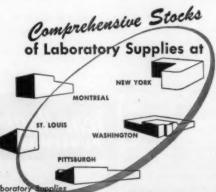
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Primary Publication

ONG ago Michael Faraday said that there are three necessary stages of useful research—to begin it, to end it, and to publish it. At the present time the first two stages are within the control of the individual scientist, particularly in view of the large amounts of money available for research and development in this country. The third step is now, more than ever, the stumbling block for the individual scientist, since he depends upon the technical journals in his field. Publishers of these journals do not have enough income to print all the papers they accept. Sources of income for publication have not increased at the same pace as the sources of funds for laboratory research. Revenue for the journals cannot be appreciably enhanced by raising society dues and subscription prices, for every increase in dues means a loss of nonpublishing subscribers, and this loss increases exponentially with the price.

Other sources of income and new means of decreasing costs must be found, because there is an ever-increasing backlog of acceptable papers awaiting their turn for publication. A few journals have not yet felt the full pinch, but others have been tormented by income deficiencies for five years or longer. When this problem was discussed in February 1950 at the National Research Council's Conference on Primary Publications, the conference recommended that data on the backlog be obtained. Representatives of 22 journals of original publication and three review journals agreed to supply the figures. Here are the averages, with the figures for the two categories in the order given above:

Pages published in 1939—1174, 805; in 1949—1555, 969; average number of pages per paper in 1939—6.8, 31.7; in 1949—6.9, 37.7; time between receipt of paper and acceptance—2.6 months, 1.0 month;

time between acceptance and publication—5.0 months, 9.7 months. This small sample is subject to a number of biases, the most apparent being inclusion of a disproportionate number of journals with good incomes and with reserve funds. However, the increase in the number of pages in a decade is certainly significant. The differences in the length of the papers are not significant, but it should be noted that many journals have increased the total words per page by using larger pages, smaller type, and double columns. Some of the indicated backlog is normal, but certainly almost 75 per cent of it is not.

Although the figures for the backlog do not indicate a serious condition at present, the factors of fixed incomes of the journals and of increasing research expenditures have certainly not yet had their full impact. The real effect of each month of unnecessary delay in publication cannot be measured solely in terms of retarded scientific progress. No one will deny that the effect is adverse, or that the effect increases rapidly, even though the delay increases gradually.

A striking anomaly of this "era of good feeling in science" is that, whereas scientists invariably use scientific methods in solving their laboratory problems, most of them seem content to use the discursive philosophical approach of the early Greeks to problems affecting the handling of their results. Publication delay is only one of the technical information problems that plague our scientific generation. Some basic and applied research, coupled with sound experimental development, can certainly show the way to quicker and better publication. Is the progress of modern science to be paced by the pedestrian tempo of obsolete communications methods and facilities?

EUGENE W. SCOTT

Interdepartmental Committee on Scientific

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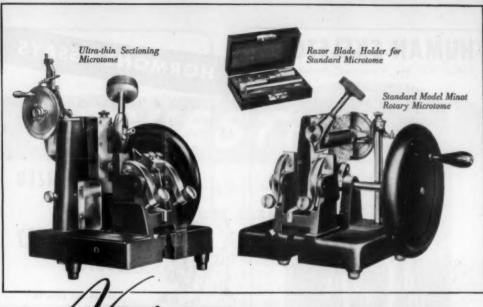
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Distance as a Factor in the Development of Attraction Fields between Growing Tissues in Culture¹

Allan A. Katzberg

Department of Anatomy, School of Medicine, University of Oklahoma, Oklahoma City

SINGLE EXPLANT OF A TISSUE when cultured in vitro in either a fluid medium or a coagulum will usually produce a pattern of growth that is distributed radially about its circumference. It has been demonstrated (1-3), however, that when two explants are placed in the same culture, the resultant growth is often organized so as to form a pattern about the axis between the two explants. The term "attraction field" has been used to describe this phenomenon.



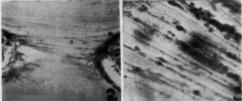


Fig. 1. 1: Attraction field photographed with polarized light, showing fibroblasts growing on fibrin strands that were rendered birefringent by the tension on the strands. × 90. 2: Stained preparation of a section cut through the attraction field area and showing the reorientation of the fibrin that composed the plasma clot and the resultant growth pattern. × 16. 3: Parallel growth pattern of cells in the attraction field. × 90.

Examination of the plasma clot in the zone between the explants by means of polarized light revealed a birefringent pattern that resembled the lines of force of a magnetic field (Fig. 1). Exploration of this area with the aid of a micromanipulator revealed that syneresis of the plasma clot had placed the fibrin strands under tension. There was also evidence of an

¹This investigation was supported by a grant from the research fund of the University of Oklahoma School of Medicine.

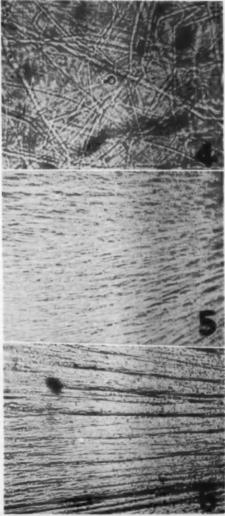


Fig. 2. 4: Fibrin strands in the zone between two explants as they appear in a freshly prepared culture, x 430. 5: Fibrin strands in the same zone, photographed after 16 hr incubation, showing some orientation. x 430. 6: Fibrin strands showing development of parallel pattern 24 hr after culturing. x 430.

Group	$\begin{array}{c} \text{Distance} \\ \text{in mm} \\ (d) \end{array}$	d_3	No. cul- tures	No. attrac- tion fields	Incidence (I)
1	0.0-0.2	.04	48	48	1.00
2	0.2 - 0.4	.16	51	49	.96
3	0.4 - 0.6	.36	50	48	.96
5	0.6 - 0.8	.64	52	48	.92
5	0.8 - 1.0	1.00	51	46	.90
6	1.0 - 1.2	1.44	52	46	.88
7	1.2 - 1.4	1.96	39	33	.84
8	1.4 - 1.6	2.56	42	34	.81
9	1.6 - 1.8	3.24	40	28	.70
10	1.8 - 2.0	4.00	48	36	.75
11	2.0 - 2.2	4.84	42	26	.62
12	2.2 - 2.4	5.76	49	28	.57
13	2.4 - 2.6	6.76	36	20	.55
14	2.6-2.8	7.84	49	22	.45
15	2.8 - 3.0	9.00	40	12	.30
16	3.0 - 3.2	10.24	38	14	.36
17	3.2 - 3.4	11.56	40	8	.20
18	3.4 - 3.6	12.96	42	2	.05
19	3.6 - 3.8	14.44	46	0	.00
20	3.8 - 4.0	16.00	38	0	.00

adhesive force between the growing fibroblasts and the fibrin, as the cells could not be separated from the fibrin strands without breaking the latter. Microscopic examination of this zone at various periods during the development of the attraction fields showed that the fibrin strands underwent a gradual reorientation from a brush-pile pattern in the freshly prepared culture to an oriented pattern after the attraction field had formed (Fig. 2).

X-ray diffraction studies (4) have indicated that tension on fibrin will produce a rearrangement of its molecules into a parallel pattern. No attempt was made in the present investigations to ascertain whether the same conditions exist in the case of attraction fields. However, these fields, composed of oriented fibrin strands, acted as a specialized roadbed which was compatible to, and preferred by, the surfaces of the membranes of the advancing filamentous processes of the proliferating cells. Each tissue explant may be considered to set up a mechanism that acts as a stimulus for the development of an oriented pattern of growth for its own cells, as well as the cells of the other explant that shared in the development of the field. It was also observed that growth apart from the zone of the attraction field was in the majority of cases very much reduced in comparison to the area of radial growth in cultures of single explants. Once the gap between the two explants was completely bridged, growth ceased.

It was also noted that attraction fields tended to develop more frequently in cultures where the distance between the two explants was relatively short. No cultures exhibited fields where the distance between the explants was more than 3.6 mm,

A series of 27 groups of cultures was prepared in which the two explants were embedded at various distances from one another. The tissues were of the

hearts of eight-day-old chick embryos, and the medium was a mixture of chicken plasma in chick embryo juice. In each culture the distance between the explants was measured with an ocular micrometer immediately after culturing. Any subsequent development of attraction fields was recorded. The cultures were classified into groups according to the distance between the explants. Table 1 lists all groups between 0 and 4.00 mm; of a total of 893 cultures, 548 developed attraction fields.

The incidence (I) as given in the table was obtained by dividing the number of attraction fields formed by the total number of cultures in that specific group. The results were plotted on a graph using the incidence (I) as the ordinate and the square of the distance (d^2) between the two explants as the abscissa (Fig. 3). The line joining the points that represent

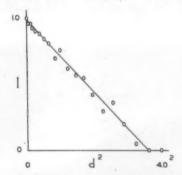


Fig. 3. Graph showing relationship of the incidence of the attraction fields (I) to the square of the distance between the explants (d2).

groups 6 and 17 forms an approximate mean for all other groups. By employing the loci of these points in the equation

$$\frac{I_1 - I_2}{d_1^2 - d_2^2} = k,$$

we may obtain the slope k, which was found to be - .0672. This represents the rate at which the incidence of the attraction fields varies in respect to the square of the distance between the explants.

The deviation (c) of the individual points from this line may be found by employing the equation

$$c = I - d^2k$$
.

The values for c very nearly approximate unity.

From these data the conclusion is drawn that the intensity of the forces that initiate the development of the attraction fields for the directional orientation of the proliferating cells varies inversely as the square of the distance between the growing tissues.

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Harold Heath, Naturalist: 1868-51

Edwin G. Conklin

Department of Biology, Princeton University, Princeton, New Jersey

AROLD HEATH, professor emeritus of zoology in Stanford University, died at his home at Pacific Grove, California, April 22, 1951, after a long illness. He was born at Vevay, Indiana, in 1868, but spent most of his school and college years with his widowed mother and his young sister in Delaware, Ohio, where I first came to know him. He was a born naturalist in the sense that he had an inherent love of and curiosity about nature, and a determination to learn all he could at firsthand. On one occasion, when he was a student in the Delaware High School, there was some disagreement in class over the number of eggs in a crow's nest. Harry disappeared at noon and returned later in the day with a crow's nest and its eggs, which he had taken from the top of a tall tree, to settle the dispute.

In his college work at the Ohio Wesleyan University, he took all the science courses and was a voluntary laboratory assistant in chemistry. When I was organizing a biological laboratory there in 1891 he became my chief assistant, and in the summer of that year he made his first visit to the seashore at Woods Hole, in part to help me gather material for my classes in zoology. As an illustration of his enthusiastic and direct approach to any problem I may cite the following incidents. I met him at the railroad station on his arrival at Woods Hole, but he left me at once and ran down to the shore, where I saw him dipping up water in his hand. I asked him what he was catching and he said, "Nothing. I just wanted to taste sea water to find out how salty it is."

Such behavior was characteristic of Heath-he was always exploring and testing for himself. Drifting in a boat over one of the pools between the islands he saw on the bottom the gorgeous spread of tentacles of a tube worm, which he later dug out of the mud in its leathery tube and brought to the laboratory, where it was greatly admired and later found to be the well-known annelid Chaetopterus, Assistant Director Bumpus asked Heath where he found it, and when others failed to find it there offered to give Heath a well-preserved specimen of Amphioxus, which he had recently brought from Naples, for every Chaetopterus he brought him. Heath went out at once and after an hour or two came back with half a dozen specimens, whereupon Bumpus called off the bargain. Chaetopterus has ever since been one of the most useful animals at Woods Hole for work in experimental

In fitting up the biological laboratory at Ohio Wesleyan, in the search for best material for classwork, in teaching the proper use of microscopes and microtomes, Heath was, I am sure, the best assistant I have

ever had. And he was such a charming fellow, so goodnatured, unselfish, and stimulating, that all who knew him in college were sorry to say "good-bye" after his graduation in 1893.

For a year thereafter he was professor of biology at the College of the Pacific at Stockton, California, and from 1894 to 1896, instructor in invertebrate zoology at Stanford. During 1896–98 he worked with me at the University of Pennsylvania, where he was one of the first group of Harrison fellows, and in the year last named he received the Ph.D. with distinction. Thereafter, he was continuously on the faculty at Stanford, first as assistant professor (1898–1901), then associate professor (1901–09), and finally full professor (1909–33), after which he became professor emeritus.

During all his years at Stanford he was closely associated with that institution's Hopkins Marine Station at Pacific Grove, where he taught in summer courses for many years, conducted his own researches and that of advanced students, and after 1925 became an all-year resident member of its staff.

His love of exploration and adventure led to his association with several expeditions to distant places, In 1906 he occupied the Smithsonian Table at the Stazione Zoologica in Naples. For several years he was acting naturalist on the U.S. Fish Commission's Albatross in her work in Hawaii, Alaska, off the coast of California, in Japan, and on a trip around the world. In 1911 he was a member of the Stanford expedition to the coast of northern Brazil. In 1913 he was sent by the U.S. Fish Commission to a point near Sitka, Alaska, to study the food of salmon. He spent the summers of 1910 and 1917 on the Pribilof Islands, in work for the U.S. government on fur-seal investigations, and it was during this last-named year that he suffered such serious injuries in a fall from a fifty-foot cliff that he was unable to take part in any further strenuous expeditions.

His research work was influenced largely by the peculiar animals collected during his explorations and by his desire to learn about their phylogenetic relationships. In his first year at Pacific Grove he found certain species of the primitive mollusk Chiton, with eggs and embryos, and he began a detailed study of their development with a view to learning about their relations to other orders of mollusks and other zoological phyla. In particular, he made a thorough study of their "cell lineage" and its relations to that of the annelids, gasteropods, and lamellibranchs, which were occupying much attention at that time. This became the subject of his first extensive paper, which he offered as his thesis for the Ph.D. degree, and which

was published in the Zoologisches Jahrbücher (V.ol. XII [1898]) in more than 90 pages of text and with five beautiful lithographic plates. This admirable study, and some six others on Chitons that followed it, tended to establish the Amphineura as the most primitive order of mollusks and to show their phylo-

genetic relations to annelids.

In his expeditions on the Albatross he had collected from dredgings in Hawaii, Alaska, and off the coast of California a beautiful lot of specimens of an aberrant and wormlike mollusk known as Solenogastre. He wrote four papers on the morphology and habits of this mollusk and a notable monograph on The Solenogastres (Memoir XLV, Mus. Comp. Zool. Harvard, pp. 179, pl. 40, with more than 400 figures [1911]).

He was also much interested in the group of beautiful pelagic gasteropods, the pteropods, and he prepared three papers on their anatomy and classification. He also prepared a monograph of some 25 pages. and 10 lithographic plates on a primitive group of bivalves, The Anatomy of Some Protobranch Mollusks (Mem. mus. roy. d'hist. nat. Belg., Deuxiem Ser.,

Fasc. 10 [1937]).

A group of bivalve mollusks of much interest to geologists for purposes of dating and identifying strata is the family of Arcidae, but the anatomy and classification of fossil forms were necessarily limited to their shells. Heath undertook a study of the anatomy of some 32 living species and thereby corrected certain errors in classification based on the shells alone. This work was summarized in a monograph entitled The Anatomy of the Pelecypod Family Arcidae, which was published by the American Philosophical Society (Trans., 31, 287-319, 22 plates [1944]). This was his last major publication. A smaller paper, with which he was much pleased, was on "A Connecting Link between the Annelida and the Echiuroidea (Gephyrea armata)" (J. Morphol., 49, [1930]).

Much of his work after his accident in 1917 had to do with material which he had on hand, or which could be found near his home; among these subjects the development of the castes in termites and their functions occupied a prominent place. In all, he published 42 articles in scientific periodicals and was a joint author with others of two books. He was a fine artist with pen and pencil and all his publications are beautifully illustrated.

In a minute prepared by one of his colleagues of the Stanford faculty, from which I am permitted to

quote, it is stated that

As a teacher he was preeminent; kindly, quizzical, and inspiring. He contributed greatly to Stanford's high position in the biological sciences. This was recognized by his "starred" position as one of the 1,000 outstanding scientists (150 zoologists) in the first edition of American Men of Science. He was a member of the Western Society of Naturalists, Phi Beta Kappa, Sigma Xi, American Society of Zoologists, and a fellow of the California Academy of Sciences. He received the honorary degree Sc.D. from his alma mater, the Ohio Wesleyan University, in 1919.

Dr. Heath married Elsie Shelley, of Son José, in 1897. She survives him, as do two sons (Ronald W. and James P.), a daughter (Phyllis Heath Walker), a sister (Mary Heath Lee), and seven grandchildren.

Technical Papers

A Possible Connection between Certain Metamorphic Phenomena and Anomalies in the Earth's Magnetic Field

John D. Weaver¹

Department of Geology, Columbia University, New York

It has long been apparent that the reference of the various mineralogical changes and orientation effects that accompany metamorphism to the two variables temperature and pressure (which in their turn are referred to depth of burial or proximity to igneous intrusions) is inadequate to explain completely the phenomena observed. In several cases, geosynclinal sediments have been buried to depths of up to 10 miles without suffering any marked metamorphic effect, whereas in other instances—as, for example, the

¹The writer is indebted to Walter H. Bucher for much helpful discussion of this subject.

young metamorphosed rocks of the East Indiesstrong metamorphism appears to have occurred without the rocks having been buried to any great depth. These examples illustrate the difficulties that are met in the endeavor to explain metamorphism on the basis of depth of burial alone.

To direct attention to additional factors that may enter into these problems, the following observations

are brought together:

1) In 1934, Visser (1), in presenting the results of his analysis of magnetic observations carried out in the East Indies, indicated that certain anomalies in the earth's magnetic field appear to be related to areas that are disturbed geophysically; in particular, he refers to the line of the Lesser Sunda Islands and the Molluccas, a line coinciding with Vening-Meinesz' line of negative anomalies. Unfortunately, observations are too few to judge the validity of this correlation, though it would seem reasonable to anticipate anomalies in the magnetic field over areas beneath which movements of subcrustal material are assumed

to be taking place.

2) Kato (2, 3), in 1933-34, published the results of a considerable number of magnetic observations in the Japanese area and showed quite clearly a direct relation between the occurrence of earthquakes, volcanic eruptions, and local magnetic anomalies. He explained the anomalies as being due to variations in the permeability of the rocks following the rise of temperature resulting from the earthquakes and eruptions. However, in the case of the Sanriku earthquakes of 1896 and 1933, he pointed to the fact that the resulting anomalous fields were in opposite directions, and the first motions of the accompanying tsunamis were also observed to be in opposite sense. This would seem to suggest that the magnetic anomalies were not caused by temperature changes, but by the movement of crustal or subcrustal material. Further support is given to this supposition by the fact that, in the case of the Mauna Loa eruption of June 2, 1950 (4), the local magnetic intensity was found to have increased considerably between May 9 and June 9, the rise probably coinciding with the beginning of the eruption. Had the anomalies been due to temperature changes, one would have anticipated a decrease in intensity.

From these observations, it would seem reasonable to infer the possibility of fairly strong magnetic anomalies over areas that are tectonically active.

3) The synthesis of mica for commercial purposes has long been a major problem. Under the pressure of war requirements, intensive research was carried out by Dietzel and others (5, 6), at the K. W. I. Ceramics Institute, Ostheim, Germany. It was found that the growth of large sheets of mica, orientated in the required directions, was greatly facilitated by the introduction of a weak magnetic field (13 gauss) at right angles to the length of the crucible containing the melt. The mica formed in large sheets parallel to the magnetic lines of force. Dietzel attributes this effect to the paramagnetism of mica. However, it was found that, although in successive experiments the iron content of the melt was reduced considerably, the degree of orientation was not affected. It is suggested, therefore, that the effect is not due to the paramagnetism of the mica, but to some directional effect of the magnetic field upon the moving ions in the melt.

Taking these various observations together, the tentative suggestion is made that a further variable which should be considered in connection with metamorphic phenomena is that of the local state of the earth's magnetic field. It is clearly possible, from Dietzel's results, that the orientation, particularly of mica minerals, may be affected by comparatively small magnetic gradients; it is suggested further that such conditions may also have some directional effect on mi-

grating ions.

It is emphasized that this suggestion is put forward very tentatively, with the object of eneouraging research in these directions, which may prove extremely useful quite apart from the validity or nonvalidity of the hypothesis.

The lines of investigation proposed are:

1) Full and detailed study of magnetic phenomena in a tectonically active area, such as the West Indies, together with field investigation of young metamorphic areas in the same general vicinity.

2) Laboratory experiments to study the effect of magnetic fields on crystallizing minerals. This study might be extended to the examination of the effects of electrostatic fields, too, since it is felt that here also may lie an enlightening field of investigation.

Studies of this sort would be too extensive and varied in their nature for one man to carry through alone, and it is hoped that other persons interested in these topics may be encouraged to undertake and intensify investigations along these lines.

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The Action of Thrombin on Fibrinogen¹

K. Laki2

National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, USPHS, Betbesda, Maryland

Investigations of the author and his associates (1-10) aimed at elucidating the role of thrombin in clotting fibrinogen have shown that thrombin is not involved in the polymerization of the fibrinogen molecules, but that thrombin acting as an enzyme makes some alteration on the fibrinogen molecule (2). It was found that the enzymic action of thrombin does not involve oxidation or reduction (3); thus it is probably a hydrolytic enzyme. Experiments with papain showed that it clots fibrinogen just as thrombin does (4), and that it is the proteolytic enzyme itself that clots fibringen (5). These experiments and the finding that the fibrin molecule, otherwise identical with the fibringen molecule (4, 6, 8-10), has a different isoelectric point (6) suggest that thrombin may split a bond, such as a peptide bond, freeing a small molecule from the fibrinogen, leaving a slightly altered fibrinogen molecule. The final proof of such a mechanism would be the finding of this predicted small molecule in the supernatant after clotting.

Since the probability always exists that a small molecule may be adsorbed to fibrinogen as an impurity and might appear in the supernatant after clotting, iodinated fibrinogen (7) was prepared and the supernatant studied for the presence of a sub-

¹ Preliminary report. Visiting scientist of the National Institute of Arthritis and Metabolic Diseases, USPHS.

stance that might have been split off by the action of thrombin. Iodinated fibrinogen differs so much from fibrinogen, and its preparation involves so many additional steps, that it is more likely to be free of possible adsorbed impurities than the original fibrinogen. Working with iodinated fibrinogen has the further advantage that it is soluble in water, clots in water, and its solution can be deproteinized by adding salt to it. It was found that the supernatant of clotted iodinated fibrinogen gave a spot detectable by ninhydrin on paper chromatograms and contained a substance that stimulated isolated frog heart,

The experimental procedure is as follows. Iodinated fibrinogen is clotted with a small amount of thrombin. In a few hours a firm gel is formed. By warming the gel it reversibly liquefies. To the liquefied gel a concentrated Ringer solution is added (final salt concentration corresponds to a Ringer solution) to remove the protein. The supernatant when tested on frog heart in contrast to similar unclotted supernatant stimulates the heart. The nature of this substance found in the supernatant of clotted fibrinogen is under investigation. Lorand (personal communication) believes that it is a peptide. Work is also in progress to find further evidence that this substance is really split from fibrinogen by thrombin and whether it is a specific heart stimulant.

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The Radiation Dose-Response Curve and Bacterial Mutations

William E. Jordan, Roy B. Mefferd, Jr., and Orville Wyss

Department of Bacteriology, University of Texas, Austin

The shapes of the curves obtained when plotting biological response against radiation dose have yielded information on the nature of the reaction. Demerec and Latarjet (1), Hollaender et al. (2), and Mefferd and Wyss (3) have shown that some induced mutations increase linearly with dose, some increase exponentially, and still others exhibit breaks in the dose-response curves. The causes of these breaks that have been observed with ultraviolet irradiation are subject to conjecture. We have observed a different type of break which is superimposed on the ultraviolet dose-response curve and also results with x-ray and

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EFFECT OF THE NUMBER OF SURVIVORS ON THE INCIDENCE OF END-POINT MUTANTS TO STREPTOMYCIN RESISTANCE IN B. anthracis

Inoculum size	Organisms inoculated	Mutante per million
	No irradi	ation
.1 ee	1.4×10^{a}	13.8
.001	1.4×10^{4}	15.0
.00001	$1.4 imes 10^{a}$	14.8
	· Irradiated	40 sec
1.0	$2.8 \times 10^{\circ}$	49.5
.1	2.8×10^{4}	50.5
.01	$2.8 \times 10^{\circ}$	17.3
.001	$2.8 \times 10^{\circ}$	17.6
	Irradiated	60 sec
1 ee	4.6×10^{4}	63
.1 ee	$4.6 \times 10^{\circ}$	20
.01 ee	4.6×10^{2}	14

nitrogen mustard treatment. This is observed when the survivors of the mutagenic action are placed in broth and permitted to grow for several generations before the assay for mutants is made. This is often done with bacteria because with a number of bacterial mutations there is considerable delay between the action of the mutagen and the appearance of the mutations in the population; with the Escherichia coli mutation to phage resistance the maximum number is not attained until each organism has made about 10-13 divisions following the application of the mutagenic agent. Consequently, in order to observe the maximum of induced mutants the bacteria surviving mutagenic action are usually placed in a condition favorable to growth before an assay of the mutants is made. With some mutations additional induced mutations appear up to 13 generations after the application of the mutagen; with others no more appear after a very few divisions. It is when these so-called end-point mutants are plotted against the dose of the mutagenic agent that a break in the curve is superimposed on the less drastic break that has often been observed with the "zero-point" mutants. This first came to our attention when doses of ultraviolet light sufficiently large to kill all but a small fraction of Bacillus anthracis spores failed to increase the incidence of mutants in a culture grown from the survivors, although lower doses gave readily measurable increases. This was especially evident when rare mutations were sought but also applies to biochemical mutants and streptomycin resistance induced by ultraviolet light as well as when x-rays or nitrogen mustard are the inducing agents.

In the experiment reported in Table 1 a population of B. anthracis was subjected to ultraviolet light as indicated. Then inocula of various sizes were removed from each treatment and planted into broth and permitted to grow for 6 hr. The incidence of streptomycin-resistant mutants in the resulting population in unirradiated cultures was not affected by inoculum size. When .1 cc of the organisms that were irradiated for 40 sec was planted, the population resulting after 6 hr contained 50.5 streptomycin-resistant mutants per million cells; but when the equivalent inoculum was planted after 60 see exposure, the incidence of mutants in the resulting population dropped back to that of the control. This is not the true incidence of mutants in the population, since a culture grown from an inoculum of 1 ee of the organisms irradiated for 60 sec had a mutation incidence of 63.0/million. Since 63 mutants/million is 1 mutant/16,000 cells, it is evident that in .1 cc of the cultures irradiated for 60 see there were only 4,600 cells, and consequently no mutants to be transferred in the subculture.

The same situation holds in the organisms irradiated for 40 sec when .01-cc transfer was made to subculture. The mutation incidence then drops to that determined by the spontaneous mutation rate.

With bacterial mutations that occur at a low rate a study of the progeny of the survivors of a large dose of mutagen may fail to reveal the mutagenic action.

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Electrophoretic Comparison of the Serum Proteins of Normal and Diethylstilbestrol-treated Cockerels1

R. E. Clegg, P. E. Sanford, R. E. Hein, A. C. Andrews, J. S. Hughes, and C. D. Mueller Department of Chemistry, Kansas State College, Manhattan

Variations in the calcium, phosphorus, and total protein of chicken and pigeon serums during the normal reproductive cycle have been repeatedly reported (1-3). Riddle and McDonald (4) indicated that similar fluctuations occurred in pigeons injected with diethylstilbestrol, and McDonald and Riddle (5) showed that the injected estrogen had the same effect on the calcium and phosphorous partition in the serum of the nonlaying pigeons as was found during normal egg production. Brandt, Clegg, and Andrews (6) demonstrated a marked difference in the electrophoretic pattern of laying and nonlaying chickens. The electrophoretic pattern of the laying hen contained an extra component and, in addition, had a much higher percentage of the slower moving globulin components. Since Riddle and McDonald were able to demonstrate a parallel in the calcium and phosphorous partition in laying and estrogen-treated pigeons, the possibility that a similar parallel exists in the serum proteins of laying hens and diethylstilbestroltreated cockerels bears investigation.

In the preliminary investigation diethylstilbestrol ¹ Contribution No. 451 of the Department of Chemistry and Contribution No. 194 of the Department of Poultry Hus-bandry, Kansas State College, Manhattan.

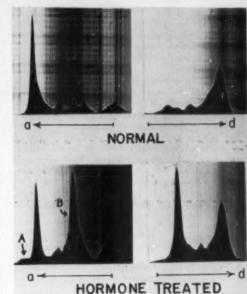


Fig. 1. Electrophoretic comparison of the serum proteins from normal and estrogen-treated cockerels. Schlieren diagrams in borate buffer (pH 8.6) after 7,200-sec electrophoresis.

pellets were implanted in both male and female chicks 8-10 weeks of age. At the end of 7 days blood was obtained from the wing vein, and the serum was prepared by mild centrifugation of the blood clot. A determination of the total calcium of this serum and the ultrafiltrate prepared from it demonstrated a partition similar to that of laying hens. Therefore the action of the estrogen was fairly rapid, and 1 week was sufficient time for the effect to be noticeable.

For the electrophoretic analyses of the serum proteins of normal and diethylstilbestrol-treated birds, two groups of 8-week-old cockerels were employed. Diethylstilbestrol pellets were implanted in the necks of 5 birds. The other birds were used as controls. One week after the implantation the birds were sacrificed, and the serum prepared from the blood was subjected to electrophoretic analysis conducted in the same manner as described in a previous publication (6). All analyses represent individual chickens; serum samples were not pooled.

A typical electrophoretic pattern of the serum protein components of the normal group (Fig. 1) was similar to the pattern obtained previously when the serums of cockerels, nonlaying hens, and young chicks were analyzed (6). On the other hand, the electrophoretic pattern of the serum proteins of the group treated with diethylstilbestrol was remarkably similar to the pattern obtained when the serum of laying hens was employed. The fast-moving component, A, previously found in the pattern of the serum of laying hens was clearly evident in the patterns of the diethylstilbestrol-treated cockerels, and, in addition, the increase in size of the slower moving components, 'B, paralleled the increase previously shown to occur when pullets begin egg production (6). In the one case attempted, the same serum protein changes were observed in a 2-year-old male bird that had been treated with the hormone.

These results demonstrate that the injection of diethylstilbestrol will cause changes associated with egg formation to occur in the serum proteins of male birds. As previously mentioned, similar changes have been noted in the total calcium and phosphorus and in the calcium and phosphorus partition of pigeon serums. From these results it can be concluded that the increase in the serum proteins, which binds the increased calcium in the laying hens so that the total diffusible calcium remains constant, may be caused by the female sex hormone. The properties of the protein fractions found in the serums of normal and estrogentreated male birds are under investigation.

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Carbon Dioxide and Root Hair Development in Anacharis (Elodea)1

Hugh M. Dale²

Department of Botany, University of Toronto, Toronto, Canada

Considerable interest has been shown in the fact that the normally hairless roots of Anacharis become coated with root hairs when they penetrate the mud. In a recent paper (1) two attempts at explanation are reviewed. In the first, soil particles are regarded as a stimulus and, in the second, light is considered the deciding factor. Cormack (2) and King (3), by completely excluding all light, reported abundant production of root hairs in water alone.

In an effort to understand the effect of light on the root, Cormack made a microscopic study. Unlike the roots grown in light, those grown in darkness had no cuticle. He assumed that the toughness of the cuticle prevented the extension of the epidermal cells as root hairs. Roots grown in the light had chloroplastids in the epidermal cells, whereas these were absent in roots grown in the dark. Lee and Priestley (4) had pointed out that the saturation of fats by

oxygen is one stage in the formation of cuticle. Unsaturated fatty materials migrating to the surface in the presence of oxygen would be toughened into cuticle. Cormack considered the oxygen produced in the epidermal cells of the root during photosynthesis to be involved in this reaction. In the absence of light no oxygen would be produced, and the unsaturated fats would wash away without being changed. He tested this by administering ethylene gas to inhibit chlorophyll formation. After this treatment the usual stains gave no evidence of a fatty layer, and root hairs were produced in the light.

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While investigating the development at the stem apex, the writer has frequently grown the cultivated and native Anacharis in nutrient solutions of high carbon dioxide tension. A continuous stream of minute bubbles of this gas flowed through the solution in covered 4-liter Pyrex jars. Under this treatment the green roots of Anacharis grown in light were invariably covered with root hairs. There was an abundant supply of oxygen, for as soon as the carbon dioxide tension built up the sprigs were buoyed up by the increased oxygen in the air spaces, and it was necessary to weight the plant down by pierced sections of glass slide to keep it immersed. Presumably carbon dioxide concentration is often the limiting factor in photosynthesis. On staining with Sudan IV, a fatty layer on the outside of the roots was observed, the root hairs breaking through this layer. This would seem to contradict Cormack's evidence; nevertheless, a study of the nature of this fatty layer was undertaken. On warming sections of the roots in 10% potassium hydroxide, the hairless root lost only a small part of its staining film, whereas the root grown in high carbon dioxide tension completely lost its coating of fatty material, which therefore could not be considered as cuticle. To discover if the fats were oxidized, a 1% aqueous solution of osmic acid was used. It is reduced and blackened if the fats are unsaturated. Soaking sections of hairless roots in the solution overnight produced a slight darkening on the outside of the fatty layer. Only a very thin outer layer was still unsaturated. The hairy roots produced in abundant carbon dioxide showed a definite blackening in the whole thickness of the layer. After saponification with the alkali no darkening of the epidermal walls occurred in either hairy or hairless roots, although the cuticle was still retained on the latter. The carbon dioxide in some way had prevented the oxidation of fats to form a cuticle, and the formation of root hairs was not prevented.

Another problem presented by the high carbon dioxide tension is that of pH. Cormack (5) in his investigations on Brassica has shown that the formation of root hairs is linked with the change of pectic acid to calcium pectate in the outer wall of the epidermis. He demonstrated that this took place in cells having a pH above 5.8, none developing on cells of a pH of 4.6-4.8. In the writer's experiments the pH of the solution in which the plants were grown was 3.8. In order to understand this discrepancy, a crude attempt

¹The investigation was made possible through the encouragement and interest of H. B. Sifton and the financial assistance of the Department Veterans Affairs, Canada.

² Present address: St. Andrews College, Aurora, Ontario, Canada.

was made to measure the pH very close to the plant. The plants were removed from their jars and given a quick shake, and the film of water on their surface was centrifuged off. The pH was found to be 0.5-1.0 above that of the surrounding medium and of the whole crushed plant. The pH of the epidermal cells must presumably be even higher, as the cell walls contain calcium pectate. Ruthenium red gave the characteristic stain even after heating sections for one hour in 2% ammonia at 90° C, which would remove any pectic acid or pectin.

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The Inhibitory Effects of Sorbose on Fungi¹ H. L. Barnett and V. G. Lilly

Department of Plant Pathology and Bacteriology. West Virginia University, Morgantown

The fungi vary greatly in their ability to utilize different sugars as sources of carbon. Few fungi have been reported as being unable to utilize glucose or maltose (1-3), both of which are common, naturally occurring sugars. The utilization by certain fungi of other common sugars has been studied extensively (4-9). On the other hand, little is known of the utilization of the so-called rare sugars and of those that are not common in nature. Sorbose is one of the latter. It is formed from sorbitol, by the action of Acetobacter suboxydans (10). When present in a medium as the sole source of carbon, sorbose is utilized well by some fungi but only poorly or not at all by other species.

An unusual inhibitory effect of sorbose on the utilization of an available sugar, such as glucose, maltose, or sucrose, was discovered when certain fungi were grown in media containing a combination of sugars. The results of these studies are presented be-

The basal medium used was composed of asparagine 2 g, KH₂PO₄ 1.0 g, MgSO₄ 7H₂O 0.5 g, microelements as sulfates, Fe 0.2 mg, Mn 0.1 mg, Zn 0.2 mg, thiamine 100 µg, biotin 5 µg, and double-distilled water, 1,000 ml. Unless otherwise stated the amount of each sugar was 20 g/l. The media were adjusted to a pH of 6.0 (except in the study of the effects of pH), dispensed in 25-ml lots into 250-ml Erlenmeyer flasks, and autoclaved at 15 psi for 15 min.

The media were then inoculated, using uniform amounts of actively growing mycelium on agar, and thus eliminating any possible effects resulting from restricted or delayed spore germination. The cultures were incubated in a constant-temperature room at

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TABLE 1

GROWTH OF 10 FUNGI IN 25-ML LIQUID MEDIA CONTAINING SINGLE SUGARS OR MIXTURES OF SUGARS (Av dry wt of 2-4 cultures grown at 25° C)

Fungus	Days	Glueose	Glucose- sorbose	Maltose	Maltose- sorbose	Serbose	Glucome (40 g/l)
Ceratostomella			-				
fimbriata	5	113	T*	84	T*	T.	107
Chaetomium							
globosum	12	373	292	364	25	T	375
Alternaria							
solani	8	99	81	140	33	20	196
Sphaeropsis							
malorum	5	153	140	166	61	T.	240
Endothia	-						
parasitica	9	201	281	191	162	11	167
Choaneophora	-	-					
cucurbitarum	5	75	104	44	46	To	100
Polyporus versicolor	9	152	232	126	192	47	221
Aspergillus	9	192	202	120	192	41	221
rugulosus	13	239	439	200	221	189	448
Botrytis	10	402	400	200	661	100	330
cinerea	9	182	266	210	310	198	379
Fusarium		-02	_00	-20	0.10	200	210
tracheiphilum	4	209	218	205	247	183	264

* T = trace of growth, estimated as less than 10 mg.

25° C, except in temperature experiments, when refrigerator-incubators and water-jacketed incubators were used. Replicates of 4-10 cultures were used, and 2-6 cultures were harvested at the same time. Harvests of mycelium were accomplished by filtering the excess liquid through a fine cloth, drying the mycelial mats at 90° C for 12 hr, and weighing.

When a number of fungi were grown on sorbose, alone or in the presence of other sugars, it was noted that the response varied greatly. In general, the fungi fell into three groups: (1) growth on maltose greatly inhibited by the presence of sorbose, with little or no growth on sorbose alone; (2) growth on maltosesorbose medium approximately the same as on maltose alone, but growth quite poor on sorbose alone; (3) fair to good growth on sorbose, as compared to maltose and maltose-sorbose media. The growth of representative fungi on different sugars is shown in

C. Ambriata showed the greatest inhibition by sorbose. Under no condition did the cultures make more than 10-15 mg of mycelium in media containing 20 g sorbose/l, even in the presence of glucose or maltose. Additional experiments not reported here showed that smaller amounts of sorbose in the presence of glucose or maltose caused less inhibition. It is apparent that the presence of sorbose in the medium actually interferes with the absorption or the utilization of glucose and maltose by some fungi. It is also evident from Table 1 that the inhibition due to sorbose is greater in combination with maltose than with glucose.

The effect of temperature was then determined by culturing fungi previously shown to be inhibited by sorbose at temperatures ranging from 15° to 35° C.

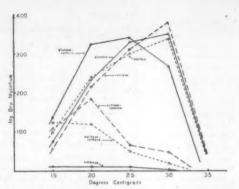


Fig. 1. The effects of temperature and the presence of sorbose on the growth of C. globosum.

The growth of C. globosum under these conditions is shown in Fig. 1. This figure shows that sorbose alone is not utilized, for no more than a trace of growth was produced at any temperature. There was little or no difference in the utilization of glucose, sucrose, or maltose when used alone. When these three curves are compared with the growth curves in media with these sugars plus sorbose, two general facts are revealed: (1) The inhibition of utilization of sucrose and maltose is greater than that of glucose. In fact, greater growth occurred on glucose-sorbose than on glucose at the lower temperatures. (2) The inhibition is increased with an increase in temperature from 20° to 25° and 30° C.

Other species, including Sphaeropsis malorum, Sordaria fimicola, and Alternaria solani, showed the same general response to increased temperature, but the degree of inhibition varied with the species. C. fimbriata failed to make more than a trace of growth in any medium containing sorbose at any temperature.

Fig. 1 also shows that the optimum temperature for growth of C. globosum is definitely dependent upon the sugars in the medium. In the absence of the inhibitory action of sorbose, growth was most rapid at 30° C. The increased inhibition of sorbose at this temperature more than balances, however, the tendency for increased growth. The net result in a mixture of sugars containing sorbose is more rapid growth at 20° C than at 30° C.

The effect of the hydrogen ion concentration of the medium can be considered only briefly. Media were prepared with the initial pH adjusted to 3.0, 4.0, 5.0, 6.0, and 7.0. C. globosum and S. fimicola grew on maltose media with the initial pH as low as 4.0. On maltose-sorbose media, growth of both fungi occurred at initial pH of 5.0 and above, but not at 4.0 or 3.0. Although the pH limits favoring growth in sorbose media appear to be narrower than those for growth in the absence of sorbose, these limits are not sufficiently narrow to account for the poor growth in the presence

One obvious effect of the presence of sorbose in the medium was the change in the type of growth. In sorbose media the colonies often remained separate, rounded, and even pelletlike, whereas in the absence of sorbose the mycelium was extensive. Microscopic examination revealed that mycelium growing in sorbose media was excessively branched. The most severe inhibition occurred in sorbose media, in which only traces of growth were present. Not only was hyphal extension inhibited, but many of the tips, particularly the apical cells, were killed. Staining the mycelium lightly with phloxine permitted counting the dead and living hyphal tips. C. fimbriata showed 77% and 15% dead hyphal tips in sorbose medium and maltose medium, respectively. In the same order and in the same media, 50% and 23% of the hyphal tips of C. globosum were dead. A. solani showed but few dead tips in sorbose medium, but excessive branching was evident.

It is thus evident that the presence of sorbose, a sugar poorly utilized by many fungi, may inhibit the utilization of a second sugar which alone is readily utilized. The reasons for this inhibition are not clear. The effect of temperature indicates that it might be based on enzyme activity or an absorption process. On the other hand, the killing of a high percentage of the hyphal tips suggests a toxic action of sorbose.

This study of sorbose utilization and inhibition of growth by sorbose is being extended, and further work is in progress. The results will be published elsewhere.

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Rapid Acclimatization of Insects to Anoxia, with Special Reference to the Housefly

F. W. Stemler and W. A. Hiestand Department of Biological Sciences, Purdue University, Lafayette, Indiana

In studying the effects of rapid ("explosive") decompression on insects and certain related forms, the writers have observed that insects form a tolerance to anoxia when repeatedly decompressed. Acclimatization appears to be an anoxic response, as is shown by the fact that repeated exposures to a nitrogen atmosphere also effectively produce a tolerance. Moreover, it has been observed that a cross-tolerance can exist between nitrogen anoxia and decompression anoxia such that a preliminary exposure to either influence will create tolerance to the other. Thus, if a housefly (or possibly any insect) is exposed for 3 min to explosive decompression at 0.2-0.15 mm Hg pressure and 10 min later is exposed to an atmosphere

of nitrogen, it will survive longer in the nitrogen than it would if exposed to nitrogen without having been previously decompressed. The reverse is likewise true; i.e., if the housefly is first exposed to nitrogen for 3 min and 10 min later is exposed to decompression, it will survive longer under decompression than if it were only decompressed without being previously exposed to nitrogen. By "survival" we mean the time from the beginning of exposure until the last visible movement of any part of the insect's body or ap-

We have measured survival to repeated decompression in 5 orders of insects, Diptera, Hymenoptera, Coleoptera, Hemiptera, and Lepidoptera, and have found that each order showed acquired tolerance to anoxia. Larvae of insects as well as adults show acclimatization. All adult species show some tolerance in 10 min time-i.e., with the second decompression. Tolerance to anoxia persists apparently for hours, for we have found that the housefly, Musca domestica, still retains some acquired tolerance for as long as 48 hr (Table 1).

Further evidence that the tolerance is produced by anoxia is shown by submerging houseflies under water.

TABLE 1 SURVIVAL TIME IN SECONDS OF 6 M. domestica EXPLO-SIVELY DECOMPRESSED AT 25° C AT PRESSURES OF 0.2-0.15 MM HG AT INTERVALS OF 0, 10, 20, AND 30 MIN

Fly No.	0 min	10 min	20 min	30 min
1	7	11	27	23
2	6	21	20	33
3	8	31	40	37
4	15	20	27	22
5	4	23	26	24
6	8	27	30	30
Average	8.0	25.5	28.3	28.1

* The housefly is characteristic of other insects in showing developing tolerance to repeated decompressions. These 6 flies represent a random sample, not being chosen for simi-

If flies are kept submerged for 3 min after all movement has ceased and then removed and dried and allowed to recover, they will survive the first explosive decompression about 3 times as long as will flies not submerged under water. In fact, the average survival time of flies previously submerged for 3 min is 23 sec as contrasted to 7.8 sec for the controls.

Detached legs of insects placed in the decompression chamber occasionally showed slight movements, although these were rarely seen and did not appear to be the same type of movements as those of the intact insect. They were much slower and required a longer period of decompression for their appearance.

The decompression chambers in which the flies were placed were the rounded bottoms of culture tubes cut off at appropriate lengths to accommodate the insects. Through a rubber stopper placed in the open end of the chamber a glass stopcock was connected with a vacuum pump. The stopcock shut off the insect cham-

ber until time for explosive decompression. With the vacuum pump running, the stopcock was quickly opened, causing sudden decompression. With the pump in operation, time was determined to the closest second until the last visible movement was seen.

In spite of investigations of the effects of reduced barometric pressures on insects (1-6) it appears that no one has reported the acquisition of tolerance to anoxia. The authors offer no explanation for acquired tolerance in insects. It probably is a cellular adjustment and it appears to be anoxie, as it results from either the anoxic anoxia of nitrogen or explosive decompression. It occurs if the interval between the first and second decompression is only 10 min or several

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The Antihypertensive Influence of Certain Sulfhydryl Compounds1

Henry A. Schroeder

Hypertension Division, Department of Internal Medicine, Washington University School of Medicine, St. Louis, Missouri

During an investigation of the effects on blood pressure of various compounds, it was noticed that certain substances containing sulfhydryl groups appeared to exert a specific depression upon the hypertension of rats (1). A differential action was observed in that the blood pressure of normotensive rats was not lowered. In addition, the response to a number of natural pressor agents was abolished or markedly diminished.

Rats were made hypertensive by partial constriction of one renal artery, a method which in our hands has been effective in two thirds of animals, Systolic blood pressure was measured in unanesthetized animals by the foot-cuff method (2), a photocell being used as an indicator. After hypertension had become established (3 weeks), blood pressure was measured under anesthesia directly with a Hamilton optical manometer while the test substances were injected intravenously (3). To evaluate the discriminative effect of a compound, depression of diastolic pressure 12 mm Hg or more 20 min after injection was chosen as the criterion. Table 1 shows the action of various sulfhydryl compounds when tested in this manner. Apparently those with a straight chain of 3 carbon atoms were antihypertensive in the sense that they lowered blood pressure acutely in hypertensive animals but did not in normotensive ones. The maximum effect developed slowly, contrary to the usual rapid action of most depressor drugs, and lasted for the duration of the

1 Work performed under a grant-in-aid from the National Heart Institute of the National Institutes of Health, USPHS.

TABLE 1

EFFECT OF SULFHYDRYL COMPOUNDS ON DIASTOLIC BLOOD PRESSURE OF NORMOTENSIVE AND HYPERTENSIVE RATS

		Normotensive				Hypertensive				
Compound	Dose (mg)	No. expt.	Av chan (mm I	ge	No. with fall • (12 mm Hg) *	No. expt.	Av change (mm Hg)	No. with fall (12 mm Hg)*	Remarks	
Cysteine	2-5	5	-	1	0	6	- 20	4		
β-Mercaptopropionic acid	5-10	5	1	0	0	8 5	- 18 0	6	With normal B P	
Thioglycolic acid Mercaptosuccinic acid	5-10 5-10	3 2	- 1	1 5	1 0	5 2	-40 -28	5		
2-Mercaptothanol	2-20	5		0	2	5	0	1	Unstable	
Thiosalicylic acid	5-20	4	- 1	5	1	4	- 4	1		
1-Methyl 2-mercaptoimidazole	5-20	4		4	1	6	- 5	1		
1,2 Mercaptobenzoxazole Sodium 2-mercapto-5	5-20	4	-	7	2	5	0	0	In propylene glyco	
benzothiazole bisulfonate	5-15	1		3	0	3	- 3	0		
Pseudothiohydantoin	5-15	4	1	0	- 1					
Thiosemicarbazide	10-20					2	-30	2		
Glutathione	10 - 20	5		0	1	- 8	- 5	0	Reduced	
Methionine	2-20	4		0	0	9	+ 2	1		
Cystine	2-20	3	-	6	1	10	- 5	2		

^{*} Ten minutes after injection.

experiment. In normotensive animals these substances were either inactive or pressor. The blood pressure of animals exhibiting hypertension in the unanesthetized state and normotension under anesthesia was not affected by sulfhydryl compounds.

The substances that appeared to exert this specific action on the hypertension of rats were sodium thioglycolate, β mercaptopropionic acid, cysteine, 2,3-dimercaptopropanol, mercaptosuccinic acid, and mercaptopyruvic acid. Substances that did not exert this action were 1-methyl 2-mercaptoimidazole, mercaptosalicylic acid, and several benzothiazole compounds. It will be noted that those substances responsible for

antihypertensive actions contained sulfhydryl groups on the ends of chains of 2 or 3 carbon atoms, whereas inactive ones were either cyclic structures with the SH group on a ring or in the middle of a carbon chain. Substances with S—S groups, such as cystine, methionine, and oxidized glutathione were inactive; reduced glutathione gave equivocal results in preliminary experiments.

The doses employed were relatively large: 5-10 mg/rat (20-40 mg/kg). Minimal doses did not result in the antihypertensive effect. The duration of the normotension was long (up to 3 hr) in brief experiments.

TABLE 2
Inhibition of Pressor Action in Rat by β-Mercaptopropionic Acid*

Pressor substance		Control		After injection of 10 mg mercaptopropionic acid					
	No. injec- tions	Av dose (γ/rat)	Av rise diastolic pressure (mm Hg)†	No. injec- tions	Av dose (γ/rat)	Av rise diastolic pressure (mm Hg)†	No. with complete inhibition (< 5 mm Hg)		
Nor-epinephrine	12	0.3	27 36	4	0.3	10	1		
11	6	0.7	36	11	1.0	8	4		
Epinephrine	7	0.4	23	5	0.8	12	0		
Arterenone	5	0.5	19	3	0.7	8	2		
Tyramine	3	33.0	13	7	56.0	5	6		
Pherentasin	3	0.2	19	3	0.2	5	1		
Angiotonin	4	0.2 ml	26	6	0.4 ml	12	3		
Isoamylamine	6	50	18	4	50	14	0		
Phenethylamine	3	70	6	4 2	70	4			
Tryptamine	3	100	56	2	100	34	0		

[•] These data represent experiments on 34 rats.

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[†] Average of peak rises.

Unanesthetized hypertensive rats were given 2,3-dimercaptopropanol intramuscularly at daily intervals. Reduction of blood pressure to normotensive levels occurred for 2 and 3 hr but not for 4; no permanent hypotensive effect was attained unless pyruvic acid was also given, in which case the rats died after several days with hypotensive levels of pressure.

A further property of sulfhydryl compounds of interest to the problem of hypertension lay in their ability to render rats insensitive to many naturally occurring pressor substances. The material employed to explore this action was, in most experiments, β-mercaptopropionic acid; other similar compounds, with the exception of cysteine, also exhibited this activity. A pressor dose of one of several naturally occurring or closely allied amines was inactive in an animal previously prepared by the intravenous injection of some sulfhydryl substances. The antipressor effect could be overcome only by giving excessively large doses of the pressor agent. The action of the following pressor amines was abolished or markedly depressed by prior injection of β-mercaptopropionic acid: norepinephrine, epinephrine, arterenone, tyramine, angiotonin (hypertensin), and pherentasin, the pressor substance obtained from human hypertensive blood (4). The action of the following was not inhibited: isoamylamine, phenethylamine, and tryptamine. It will be remembered that all the compounds inhibited by the sulfhydryl substance (except angiotonin, the formula of which has not yet been discovered), contain either hydroxyl or carbonyl groups; those not affected do not contain these groups. The order of magnitude of inhibition is shown in Table 2. Inhibition of pressor action occurred in both hypertensive and normotensive rats, the blood pressure of the latter being unaffected by the sulfhydryl compound (Fig. 1).

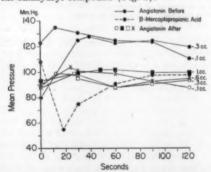


Fig. 1. Suppression of response in the rat of a pressor agent Fig. 1. Suppression of response in the rat of a pressor agent (in this case angiotonin or hypertensin) by a sulfhydryl compound. The lines indicate mean blood pressure calculated from Hamilton manometric photokymographs. Injections were made at zero time. Note the almost complete inhibition of the response to the pressor substance, even in larger doses, after the injection of the sulfhydryl compound (in this case β-mercaptopropionic acid neutralized to pH 7.4 with sodium bicarbonate). The solution of angiotonin (hypertensin) was editated to such a strength that 0.1 cc. avec a minimal pressure. adjusted to such a strength that 0.1 cc gave a minimal pres-sor reaction. These curves are typical of those obtained with other pressor agents. Pulse pressure was relatively unchanged by the sulfhydryl compounds and by the pressor agents sub-sequently injected.

Lowering of blood pressure in chronic renal hypertensive dogs was obtained by both 2,3-dimercaptopropanol given intramuseularly and β-mercaptopropionic acid given intravenously. In one experiment reduced glutathione appeared to cause a slight effect. The durations of the changes were short (2-4 hr), and were sometimes followed by hypertensive reactions. In hypertensive patients, 2,3-dimercaptopropanol given in doses of 100-150 mg intramuscularly also lowered blood pressure temporarily (11/2-4 hr), although the usual response of normal subjects is elevation of blood pressure (5). Repeated doses apparently caused depression of blood pressure for several days in a few subjects. As in dogs, occasionally hypotensive responses were followed by hypertensive ones. Cysteine in doses as high as 2.0 g intravenously exhibited little or no effect.

From these experiments it appears that the administration of certain sulfhydryl compounds of simple molecular structure can cause temporary lowering of blood pressure in experimental and human hypertension without affecting normal blood pressure similarly, Furthermore, the pressor action of a number of naturally occurring amines is markedly depressed. The application of these findings to the control of human hypertension deserves further study.

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The Distillation of Lithium Metal

Leo F. Epstein and W. H. Howland

Metallurgy Department, Knolls Atomic Power Laboratory,¹ General Electric Company, Schenectady, New York

If a piece of lithium is heated in air in a glass test tube, the metal first darkens because of the temperature-accelerated reaction with the nitrogen, oxygen, and other constituents of the air. At, or a little above, the melting point (1) 186° C, a spectacular reaction with the glass occurs. The test tube grows red, then white hot. In a short time, the bottom falls out of it and the metal burns with a brilliant white flame, like that of magnesium. It has been reported (2) that the lithium in this reaction reduces the SiO2 and silicates of the glass to form lithium silicide. Attempts to purify Li on a laboratory scale by distillation in glass have usually ended in failure, accompanied by a fireworks display similar to that described above. It is the purpose of this paper to show how a glass system can be used to carry out this process.

¹The Knolls Atomic Power Laboratory is operated by the General Electric Company for the Atomic Energy Commis-sion. The work reported here was carried out under contract No. W-31-109 Eng-52.

As early as 1900 Kahlbaum (3) reported that he had successfully distilled Li in a glass system. This reference, which appeared in a rather obscure Swiss journal, seems to have been largely overlooked by subsequent workers. The trick is to keep liquid Li from coming into contact with the glass; the dilute vapor apparently does not react readily. (Whether this is due to the concentration of Li (g, Li/cm3) being less, or whether the rapid reaction of the liquid metal with glass is due to the ubiquitous oxide and nitride impurities, is not known.) Kahlbaum carried out the distillation at a few hundredths of a micron pressure by putting the Li in a silver crucible inside a glass system. The glass walls, on which the vapor condenses, must be kept relatively cool; and this requires a rather delicate heat balance and careful dimensioning of the system, so that the heat applied to the bottom of the tube does not cause an excessive temperature rise in the glass walls, above the metal crucible, where the distillate is collected. The ideal way to carry out this step is by induction heating (which does not raise the temperature of the nonconducting glass significantly). Using a G-E 2-kw electronic heater, operating at about 500-600 ke, and a Type 347 stainless steel cup (instead of silver), a beautiful Li mirror can be deposited on a Pyrex glass tube. In this process, care must be taken to prevent spattering of the liquid Li on the glass walls, particularly upon initial melting; and for this purpose it has been found convenient to weld a "chimney" with baffles over the metal cup. It should be noted that because of the low molecular weight of Li vapor, this and other welds must be extremely tight, and to test this, an He mass spectrometer leak detector has been most

To distill larger quantities of Li, a stainless steel "cold finger" about 1.5 cm in diameter was sealed into a large ground-glass joint by the use of Fernico. This was fitted to the glass distilling tube, about 4 cm in ID and 35 cm long, and cooled with dry ice (solid CO2). In this way the distilled product collected largely on the metal tube and could subsequently be readily scraped off in an argon atmosphere dry box without contamination by glass or Li-glass reaction products. Although the exact rate of heat input to the steel cup is difficult to estimate because the efficiency of coupling of the work coil to the system is unknown, the following conditions are quoted for the guidance of workers who may attempt to repeat this experiment: current 0.35 a, pressure 0.01 to 0.05 μ, temperature 450° to 500° C. Under these conditions, a distillation rate of about 1 g of Li/hr was achieved, and it has been found convenient to distill 1-2 g at a time in the system.

The resulting Li, on exposure to air at room temperature, does not react and darken rapidly as a freshly cut surface of commercial Li will, but retains a shiny and metallic luster for 10 hr or more. We have also observed in this laboratory that the rate of reaction of distilled sodium with air is markedly less than that of more impure material. The effect of

traces of impurities on the corrosion of other metals is well known; thus, for example, it is reported (4) that, whereas 99.95% pure zinc dissolves completely in 10% HCl at room temperature, in the same time under identical conditions, "chemically pure" zinc (99.99%) loses 53% by weight and "spectroscopically pure" zinc (99.999% or better) loses only 0.02%. Similarly, in a study of the dissolution rate of aluminum in NaOH solutions, Streicher (5) found that under identical conditions (0.3N NaOH, 23° C, specimen area 40.5 cm2, test period 240 min), a sample containing 0.0005% Fe as the principal impurity lost only 115 mg, whereas one containing 0.84% Fe lost 1075 mg. The observations noted above on the reactions of purified alkali metals with air are consistent with these large effects of impurities on corrosion rates in electrolytic systems.

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An Instrument for Dynamic Vital Capacity Measurements¹

Edward A. Gaensler

Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard) Boston City Hospital, and Department of Medicine, Harvard Medical School; Thoracic Surgery Service, Physiology Laboratory, Sanatorium Division, Mattapan; and Department of Surgery, Boston University School of Medicine, Eoston, Massachusetts

The vital capacity has been used for the clinical evaluation of pulmonary function for more than 100 years without any modification (1). It is recognized that this test cannot give any indication of defects of distribution or diffusion of gases. Even now, however, it is widely employed in efforts to evaluate ventilatory function concerned with the exchange of air between the outside atmosphere and the lungs. The use of the vital capacity in this connection is based on the misconception that the effectiveness of ventilation is solely dependent on the stroke volume, or the amount of air that can be moved by a single maximal effort of all the muscles of respiration (2).

Interest in applied clinical pulmonary physiology has been greatly stimulated during the past 20 years by the rapid advances in thoracic surgery and phthisiotherapy. During this time it has been increasingly

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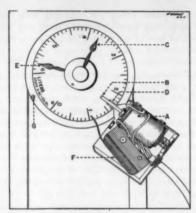


Fig. 1. Timed-capacity attachment mounted on spirometer. The cover has been removed, and changes made on the cali-brated wheel are indicated.

apparent that the effectiveness of ventilation depends not so much on the single stroke volume as on the volume of air that can be moved per unit of time. A number of investigative methods, including maximum breathing capacity, high-speed recording spirometry, air-velocity studies, and alveolar pressure determinations, have been developed to evaluate this time-volume relationship. These methods, because of the complexity and expense of the apparatus and the trained personnel required, have been largely reserved for the laboratory engaged primarily in research. The vital capacity, therefore, continues to be the most widely and most frequently used test of pulmonary function, with consequent frequent misjudgment of the degree of pulmonary insufficiency.

An attachment for the standard vital capacity spirometer has been constructed with the aim of evaluating stroke volume as well as its time relationship. It measures and records simultaneously the total vital capacity and the volume exhaled during any preset time interval from 1 to 10 sec without recourse to a kymograph and later tracing analysis. The timing cycle is initiated by the onset of the patient's maximal expiratory effort. The apparatus does not introduce added resistance in the airway, it is inexpensive, its use requires no special training on the part of physician or patient, and the test requires no more time or effort than an ordinary vital capacity deter-

The spirometer attachment.2 The unit, with its cover removed, attached to a spirometer is shown in Fig. 1. It consists of a small, plunger-type solenoid (A) and a microswitch (F), both used in conjunction with a simple electronic timer (Fig. 2). Before the test, the graduated wheel is set at zero liters, as in the usual vital capacity test. This setting impinges the small pin (G) against the lever of the normally closed micro-

² The entire spirometer or the attachment and timer may obtained from Warren E. Collins, Inc., 555 Huntington Ave., Boston 15, Mass.

switch (F) and thereby opens that switch. As the patient exhales into the spirometer, the graduated wheel turns clockwise and the pin (G) moves away from the microswitch actuator, closing the switch, which initiates the timing cycle. For the duration of the timed interval the solenoid (A) is activated by the timer, and the plunger (B) protrudes. At the end of the previously selected time interval, the plunger retracts. The standard pointer (E) indicates the total vital capacity by arrest of its motion by the customary pointer rest (D). A second pointer (C) was added the motion of which is arrested by the solenoid plunger (B) only for the duration of the timed interval. At the completion of the test the pointer (E) indicates the total vital capacity irrespective of time-in the illustration, 5,740 ml. Pointer (C) shows the volume exhaled during the preselected time interval-here 3,750 ml. Return of the calibrated dial to the zero position automatically resets the timer and spirometer for the next test.

The timer. The circuit for the timer (Fig. 2) was adapted and modified from a welding control (3). Instead of a high-vacuum tube it uses a miniature thyratron tube, whose cutoff is sharp and does not depend on a slowly rising plate current. It is therefore well adapted to timing very short intervals. The interval does not fluctuate with line voltage and is not

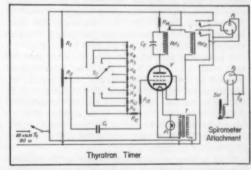


Fig. 2. Circuit diagram for thyratron interval timer and vital capacity attachment for determination of timed capacities. (Entire timer can be enclosed in a 5" × 7" × 2 1/2' chassis.)

List of components R, = 100,000-ohm, 1/4-w resistor

= 10,000-ohm potentiometer $_{3}^{2}$ - R_{19} = 180,000-ohm, $\frac{1}{2}$ -w resistor = 10,000-ohm, $\frac{1}{2}$ -w resistor

 $R_{10} = 100$ ohm, N_2 -w resistor $C_1 = 2 + x f$, 600-v oll condenser $C_2 = 2 + x f$, 600-v oll condenser $C_3 = 4 + x f$, 150-v electrolytic condenser $Rel_4 = 10.000$ -ohm, x - p, x - f, normally closed midget relay $Ret_2=115$ -v a-c, d-p, s-t, normally open midget relay Pi=6.3-v, 0.25-a pilot light $S_1=$ s-p, s-t toggle switch

 $S_{g}^{*} = 10$ -pole, single-gang, single-circuit nonshorting rotary Sa = Microswitch, BZ-2RW, with spring removed, wired nor-

mally closed Sel = Miniature solenoid, 115-v a-c, 1-oz pull, intermittent duty, modified as in Fig. 1

tent duty, moduled as in Fig. 1

Tarnansformer, 115-v-6.3-v, 1-a

P, P, = 3-prong polarized plug, male and female

V = Tube 2 D 21 (Types 2050 and 2051 may be used, requiring slightly different value for O₁)

affected by heat and humidity if a high quality oil condenser is used for C_1 . The constants given in Fig. 2 permit choice of any time interval from 1 to 10 sec in 1-sec steps. After the tube has been installed the time selector is set for 10 sec and the potentiometer R_2 is adjusted with a screwdriver until the timed interval is exactly 10 sec as checked with a stop watch. No further time adjustment is required until the tube is changed. The timer has only two external controls, S_1 , which turns the instrument on and off, and S2, which permits selection of the time interval.

The test. The timer is turned on about 1 min prior to the test to permit warming of the tube filament. The graduated dial is set at zero, the desired time interval is selected, and the patient is instructed to take as deep a breath as possible and then to exhale all the air as rapidly as possible into the mouthpiece. The dial is returned to the zero position, and the timed volume and total vital capacity are recorded. Before the test only two special precautions must be observed. The patient must be instructed to exhale all the air in his lungs as rapidly as possible. The mouthpiece used must have an internal diameter at least as large as the inlet to the spirometer; otherwise an undue resistance to the flow of air is introduced and expiration will be abnormally prolonged.

Results. A detailed clinical analysis of the timed capacity tests in normal volunteers and in patients with various types of ventilatory insufficiency will be presented elsewhere (4). The instrument has been used as a part of the routine pulmonary function work at our laboratories for the past 18 months.

A number of time intervals from 0.1 to 10 sec have been tried. The 1-sec, 2-sec, and 3-sec volumes were found to be the most significant for differentiation between various types of ventilatory insufficiency. Normal volunteers and "pulmonary normal" hospitalized patients were able to exhale on the average 83% of the total vital capacity during the first second of the vital capacity effort, 94% during the first 2 sec, and 97% during the first 3 sec.

When a 4-mm stenosis, approximately the smallest compatible with life, was introduced in the spirometer tubing, no effect on the volume of the total vital capacity was observed. However, the 1-sec volume was reduced by 84%, the 2-sec volume by 59%, and the 3-sec volume by 39%.

Patients with ventilatory insufficiency fell into two groups. Those with "restrictive" insufficiency (5) usually had pulmonary parenchymal or pleural disease or had had previous resection or collapse of pulmonary tissue. The ventilatory defect in these patients was one of reduced stroke volume, and the percentages of the total vital capacity expired during the various time intervals were essentially normal. For example, in 58 patients who had had thoracoplasty, the mean vital capacity was reduced to 61% of predicted normal, but 74% of this volume was exhaled during the first second of the effort, 89% in the first 2 sec, and 93% during the first 3 sec.

In the second group were patients with "obstructive" ventilatory insufficiency (5). They had bronchial disease or loss of pulmonary and thoracic elasticity, as in bronchial asthma, pulmonary emphysema, and anatomic obstruction of a major bronchus. The defect in ventilation here was due to abnormal resistance to the flow of air or abnormal resistance of the lungs and thorax to deformation. In these patients the single stroke volume was often nearly normal, but the expiratory velocity was markedly reduced, and the percentages of the total vital capacity exhaled during 1, 2, and 3 sec were extremely abnormal. In 28 patients with severe bronchial asthma, for example, the mean total vital capacity was 71% of predicted, but only 43% of the total volume was exhaled during the first second, 59% in 2 sec, and 71% in 3 sec.

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Results of the timed capacity tests were correlated with a number of other tests of ventilatory function. The coefficient of correlation, r, between the conventional vital capacity and the maximum breathing capacity varied from 0.24 to 0.56, depending on the number of patients with "obstructive" insufficiency included in the series. The correlation improved with the shorter timed capacities, and r between the 1-sec volume and the maximum breathing capacity was 0.88, regardless of the type of patients included in the series. In contrast to the total vital capacity, timed capacities correlated well with the air-velocity index (2) and the ratio of residual volume to total lung capacity. Furthermore, in normal volunteers and in all patients except those with bronchial asthma the percentages of the total vital capacity expired at the various time intervals varied little on repeated occasions the same day and from month to month over the course of 11/2 years.

A larger number of studies will be required to correlate clinical symptoms of dyspnea with the timed capacities and to determine whether the actual volumes exhaled at the various time intervals or the percentages of the total vital capacity are the more significant data.

The timed capacity is not suggested as a substitute for any of the more elaborate tests of ventilatory function available in the physiology laboratory. It is suggested for use in the clinic, hospital ward, and physician's office, for large-scale and screening studies, and for the study of the effectiveness of protection afforded by bronchodilator drugs. It offers a simple method for measurement of both stroke volume and effective ventilation and for differentiation between "obstructive" and "restrictive" ventilatory defects.

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Comments and Communications

The Search for Truth Versus Bigotry

SELDOM have I read what is ostensibly so fine a statement of natural science in its ideal purity, and never one so misapplied, as that of Clarence W. Metcalf (SCIENCE, 113, 696 [1951]). The title given his communication, "The Search for Truth," was taken in vain, for it was written to condone the withholding of truth from some school children. By generalities he sought to justify the New York state law—sponsored by a religious sect alleged to disbelieve in all disease—which exempts the children of this sect from school instruction in the science of health and hygiene.

"Who is to say what constitutes the "truth' claimed for 'scientific laws... established beyond a doubt?" " So runs the query and academic discussion of this man who appears as the scientist-philosopher. "There is today no avenue of scientific investigation in which the intellectually honest scientist will assert that the theories on which current investigations are conducted

have been 'established beyond doubt.' "

The writer of the above has confused established scientific facts and generalizations with the current investigations of new theories that are constantly proceeding on all borders of natural science, where there are always unknowns, and always questions and new problems. Indeed, the continuing quest for more truth is the most commendable characteristic of science.

In health science, school children hear about the gradual collapse of the medieval concept of disease, of the work of Pasteur and others establishing the germ theory of disease. They may learn a thousand and one facts—that tuberculosis is caused by a certain bacterium, diphtheria by another; that antitoxin saves life from diphtherial death; that certain mosquitoes transmit malaria; that countless people in history died of malaria; and so on ad finitum. And pupils learn of many things vital to health and life. They also learn about the developing science so that they may have the critical, cautious attitude about all things in this field, to the end that they may become wiser than their fathers.

It is an absurdity to call health science instruction "a tendency to statism, with its enslavement of body and mind to the whims of the relatively few men whose aim is to force conformity. . . ." It is rather the effort to enlighten with the facts discovered by the relatively few, for the benefit of the life and health of all, including Christian Scientists.

It is sheer rhetoric to proclaim: "Any attempt to abrogate the right of the individual citizen to refuse acceptance of a scientific theory... is an expression of bigotry. And bigotry of any nature—scientific or

religious—is intolerable to free men."

No one is forced to accept a scientific theory. On the other hand, in some unscientific sects and groups, the leaders do all they can to make their followers dis-

believe certain scientific theories and facts. They would prevent their children from knowing about them. They would keep them blind to what their American birthright would guarantee them, freedom to learn all things. They fear, apparently, that if their children learn of the findings of science, they may prefer these findings to the dogma of their fathers. Therein lies the bigotry of the elders—and bigotry is intolerable to free men.

WALTER C. KRAATZ

Biology Department, University of Akron

Hemolytic and Antihemolytic Substances in Guinea Pig Liver

In 1949 we reported that simple 0.9% saline extracts of fetal guinea pig liver possess high hemolytic activity, whereas similar extracts of the adult are inactive (1). This was followed by a paper (2) demonstrating that it is not the absence of a lysin that accounts for the inactivity of the adult extracts, but the presence of inhibitors in the mitochondria and microsome fractions of the liver cells. It was shown that, when these inhibitors are separated out of inactive adult extracts by ultracentrifugal fractionation, very active preparations are obtained. Recombining the centrifugally separated fractions restores the inactive state. That is principally what the paper was about (2).

In between the time these two reports appeared in print, Laser published a paper (3) reporting the isolation of a hemolytic substance of high activity from the serum, spleen, liver, red blood cell, and the brain of the horse, the brain and blood of humans, and the spermatozoa of hogs. He prepared this substance from such organs by a procedure involving some 14 steps, including hot ethanol and ether extraction, transference of alkali-soluble material from ether extract into 1.5% KOH solution, formation of a lead precipitate, and, finally, molecular distillation in high vacuum at a temperature of about 60° C. The end product, he reports, was a substance identified as cis-vaccenic acid $(CH_3 \cdot (CH_2)_5 \cdot CH = CH \cdot (CH_2)_9 \cdot COOH)$. These experiments of Laser's have convinced him (4) that the ether-soluble "hemolytic acid" thus isolated-for example, from the horse serum-is the same as the heat-labile lysin we described in saline extracts of guinea pig liver. Since the agent in guinea pig liver appears to be inactivated by many of the procedures used by Laser in the preparation of his "hemolytic acid," we believe it wise to leave for future investigation to determine whether there are any resemblances structurally, chemically, or otherwise between the two substances.

It was also implied (4) that we are completely unaware of the identity of some of the inhibitors in the plasma or the serum. This is contrary to the facts presented in our paper (2). What we are uncertain about is the nature of the inhibitors associated with the mitochondria or microsome fractions of the liver cell. We have no evidence, as yet, that those inhibitors are the same as the inhibitors present in the plasma or serum (i.e., albumin globulin, calcium, cholesterol, and lecithin).

There are many other discrepancies between what we actually wrote in the paper (2) and what Laser interpreted as having been written (4). Those interested are referred to the two papers in question.

DAVID B. TYLER

Department of Physiology and Pharmacology School of Medicine University of Puerto Rico

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The Decarboxylation Reaction

SEVERAL specific objections have been raised to the author's proposal (1, 2) that transitory carbanions are hypothetical intermediates in the base-catalyzed decarboxylation of alpha amino acids. Three of these objections (the first three discussed) involve emphasis on negative findings as limitations to the generality of the reaction. As such they should be considered with some skepticism. The failure of ethyl isobutyrate to undergo the Claisen condensation was long thought to impose restrictions on the mechanism which experience indicated were nonexistent. Others (the last two) are comments involving interpretations of the transitory existence, method of formation, and structure of the carbanion, and the generalized scope of the carbanion explanation.

1) The role of the carbonyl function as an acceptor. The fact (3, 4) that aldehydes fail to act as acceptors in the decarboxylation of various acids has been stated as a serious objection to the proposal that addition of a transitory carbanion to the carbonyl group of the anhydride plays a role in the decarboxylation. There are, however, decarboxylation reactions in which the aldehyde functions do act as acceptors. These are the spontaneous formation of 1-indanone on decarboxylation of o-formylcinnamic acid (5) and the base-catalyzed formation of carbinols on decarboxylation of quinaldinic acid in the presence of aldehydes (6), Both of these can be visualized as proceeding through a transitory carbanion. These reactions are much stronger evidence than negative findings, particularly in light of our finding that decarboxylation of acetylglycine, although long thought not to take place, does in fact react as other acylamido acids (2).

2) Failure of the reaction in the absence of an alpha hydrogen. The formation of a carbanion by decarboxylation does not require an alpha hydrogen. It has been reported (6), however, that a-phenyla-aminopropionic acid does not undergo the reaction,

and this has prompted the suggestion that the formation of the carbanion by decarboxylation is unlikely. The decarboxylation of quinaldinic acid in its condensations to form carbinols from aldehydes is an example of a decarboxylation reaction that requires no hydrogen alpha to the carboxylic acid function. Again, this fact indicates that negative evidence to the contrary is likely to be untrustworthy.

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3) The fact that acylamido acids do not lose carbon dioxide in the absence of an anhydride. This can be interpreted as meaning that the anhydride acts as an acceptor and in doing so provides the driving force for the reaction. One should not lose sight of the fact that the decarboxylation of acylamido acids in the presence of acetic anhydride may be a limited aspect of a general reaction. Many acids lose carbon dioxide in the presence of a base, and possibly it will be demonstrated that additions to carbonyl functions can take place in these reactions also. Hammett (7) discusses the relative roles of acceptor and reactant in providing the driving force for acid- and base-catalyzed Claisen condensations.

4) The transitory role of the carbanion. The carbanion has a transitory existence in decarboxylation (1, 2). This concept may vary from the usually accepted transitory carbanion of the aldol type of condensation to the bare possibility of existence even in the absence of resonance stabilization, which is the basis for an explanation of β-elimination reactions (8). The usually accepted statement on the transitory nature of ionic intermediates in organic reactions has been given by Hammett (9). The extent to which resonance stabilizes the carbanion raises interesting questions, because the only apparent factor involved is the inductive effect of the acyl- or sulfonyl- (12) group. This structure, RCONHCH, CO, H, is not to be compared, however, to that in which the inductive effect is transmitted through a methylene group. The amino group with its unshared electrons can aid in transmitting the inductive effect of the acyl- or sulfonyl- group to the alpha carbon. Electron-withdrawing effects of the acetamido group are not unknown. The formation of 4'-bromo-4-acetamido diphenyl ether on bromination of 4-acetamido diphenyl ether is an example of the inductive effect produced by the acylamido group (10). This group also acts as an electron donor in substitution reactions of acetanilide. It is also recognized that carbanions can be formed as transitory intermediates from compounds where apparently no resonance is involved, such as the bicyclic sulfone of Doering and Levy (11) and 3-alkylpyridines (12). It would appear from these observations that resonance stabilization of an intermediate carbanion, although of significance in terms of its possible independent existence, is not a reliable criterion for postulating its participation as the sole intermediate in a reaction mechanism. Presumably, increased stabilization would decrease the energy barrier for the formation of an intermediate by an amount equal to the increased energy barrier for the following reaction, with a net result of no obvious gain in lowering the net energy barrier.

5) Generalized concept of the reaction; oxazolones and oxazolonium intermediates. The use of oxazolone and oxazolonium structures as a source of carbanions has been considered by some (4) as a serious objection to the idea that other types of carbanions can participate in the acylamido reaction. It appears to this author that the oxazolone concept is helpful, although perhaps needlessly elaborate, in interpreting the course of the reaction in this specialized case, so long as it is not made the basis for overemphasis on the need for resonance stabilization of the carbanion. There is, moreover, considerable merit in a more generalized concept of the reaction which will coordinate the data on other decarboxylations, not all of which involve anhydride condensations. Our observations on the formation of disulfides and aldehydes on decarboxylation of sulfonamido acids (13) provide an example.

RICHARD H. WILEY

Department of Chemistry University of Louisville

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Zoological Nomenclature: Notice of Proposed Suspension of Rules in Certain Cases for Avoidance of Confusion and the Validation of Current Nomenclatorial Practice (A. (n.s.) 9)

NOTICE is hereby given that the possible use by the International Commission on Zoological Nomenclature of its plenary powers is involved in applications relating to the undermentioned names included in Parts 9/10 of Volume 2 of the Bulletin of Zoological Nomenclature, which was published on August 15,

1) Entamoeba Casagrandi & Barbagallo, 1895, Endamoeba Leidy, 1879, and Poneramoeba Lühe, 1909 (Class Rhizopoda) (action designed to validate existing practice) (pp. 243-81) (File 185).

2) dentatus Diesing, 1839 (as published in the binominal combination Stephanurus dentatus) (Class Nematoda) (question whether this name should be preserved for the kidney worm of swine) (pp. 282-93) (File 188)

3) Eysarcoris Hahn, 1834 (Class Insecta, Order Hemiptera) (proposed validation of existing nomenclatorial practice) (pp. 294-5) (File 212)

4) acuminata Ioff & Tiflov, 1946 (as published in the combination Rhadinopsylla (Rectofrontia) acuminata) (Class Insecta, Order Siphonaptera) as applied to species No. 68 (proposed elimination of homonymy caused by printer's error) (pp. 296-7)

2. The present notice is given in pursuance of decisions taken, on the recommendation of the International Commission on Zoological Nomenclature, by the Thirteenth International Congress of Zoology, Paris, July 1948 (Bull. Zool. Nomencl., 4, 51, 57 [1950]; ibid. 5, 5, 131).

3. Any specialist who may desire to comment on any of the foregoing applications is invited to do so in writing to the Secretary to the International Commission (28 Park Village East, Regent's Park, N. W. 1, Eng.) as soon as possible. Every such comment should be clearly marked with the commission's file number as given in the present notice.

4. If received in sufficient time before the commencement by the International Commission of voting on the applications in question, comments received in response to the present notice will be published in the Bulletin of Zoological Nomenclature; applications received too late to be so published will be brought to the attention of the International Commission at the time of the commencement of voting on the application in question.

5. Under the decision by the International Congress of Zoology specified in paragraph 2 above, the period within which comments on the applications covered by the present notice are receivable is a period of six calendar months calculated from the date of publication of the relevant part of the Bulletin of Zoological Nomenclature. The double part now in question was published on August 15, 1951. In consequence, any comments on the applications published in this double part should reach the secretariat of the International Commission at latest by February 15, 1952.

FRANCIS HEMMING

Secretary to the International Commission on Zoological Namenclature

Mathematicians and the California Oath

AT ITS meeting of September 4, 1950, the Council of the American Mathematical Society passed the following motion:

The Council of the American Mathematical Society deplores the harm done to academic freedom and scientific progress by the recent action of the Regents of the University of California in imposing arbitrary and humiliating conditions of employment on the faculty. The Council notes that this action has already resulted in a great discontent and loss of morale in the California faculty, and in the consequent desire of many distin-

guished faculty members to move elsewhere. The future effects of this action upon the scientific and academic work of the California faculty and upon the standing of the University will be disastrous. The Council therefore urges that the Regents reconsider their action, so as to restore academic freedom and to insure the continued high standing of the University of California.

At its meeting of September 4, 1951, the Council reaffirmed its action of 1950 and adopted also the following resolution:

Owing to the expressed reluctance of a large number of mathematicians to attend meetings of the American

Mathematical Society at the University of California on account of the conditions condemned in a resolution adopted by the Council at its meeting of September 1, 1950, the Council hereby regretfully resolves that it will not consider holding any meetings of the Society at the University of California during the calendar years 1951, 1952, and 1953 unless those conditions have been alleviated in the meantime.

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American Mathematical Society Office of the Secretary Yale University



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News and Notes

Scientists in the News

Gaylord W. Anderson, director of the University of Minnesota School of Public Health, and Walter E. Batchelder, assistant director, American College of Surgeons, have been appointed to the Caneer Control Committee of the National Caneer Institute. The 12 members of the committee represent the medical disciplines most concerned with caneer, as well as geographical areas of the U. S. and caneer interests in the states, medical schools, and private practice.

David W. Bishop, professor of physiology at the University of Massachusetts, has been granted a year's leave of absence to work at California Institute of Technology.

Raymond A. Blackmore has joined the staff of Battelle Memorial Institute and will participate in that institution's rapidly expanding radiochemical research. Dr. Blackmore until recently was associated with the "Na Churs" Plant Food Company, Marion, Ohio, as its technical adviser. Four research staff members have been promoted to supervisory positions. Horace J. Grover has been named supervisor of research on fatigue and structural analysis; Arthur D. Schwope, supervisor of research in mechanical metallurgy; Henry A. Saller, supervisor of research on special metallurgical materials; and Charles F. Lucks, supervisor of the Institute's instrument division.

George E. Boyd, associate director of the chemical division at Oak Ridge National Laboratory, has won the 1951 Southern Chemist Award. The gold medal was presented to Dr. Boyd at the general meeting of the Southwide Chemical Conference under the joint auspices of the American Chemical Society's Wilson Dam Section and the Southern Association of Science and Industry, Inc. Dr. Boyd was cited for his contributions to the atomic energy program, specifically in the development of chemical separation techniques. The Southern Chemist Award is given annually to recognize and honor distinguished service to the profession of chemistry in the Southern states and to focus national attention upon the scientific progress of the South.

James Boyd has resigned as director of the Bureau of Mines, a post he got in 1947 despite protests of John L. Lewis, president of the United Mine Workers. He has joined the executive staff of the Kennecott Copper Corporation.

Elizabeth C. Crosby, professor of anatomy, University of Michigan Medical School, will deliver the thirty-fifth Mellon Lecture before the Society of Biological Research of the School of Medicine, University of Pittsburgh, on November 6. Dr. Crosby's subject will be "Central Nervous System Control of Eye Movements."

Kenneth Dameron, professor in the Ohio State University Business Organization Department, is serving as marketing expert for a project sponsored by the Technical Assistance Division of ECA. He will confer with marketing executives in Norway, Sweden, and Denmark in an effort to acquaint them with American merchandising methods.

Gordon M. Fair, sanitary engineer at Harvard University, was awarded an honorary Doctor of Engineering degree by the Technical University of Stuttgart in ceremonies at Harvard. Professor Fair is a scientific director of the Rockefeller Foundation, which has supported sanitary engineering projects in Europe under his direction. He was recently appointed a member of the Expert Panel on Environmental Sanitation of the World Health Organization. He is Gordon McKay professor of sanitary engineering, Abbott and James Lawrence professor of engineering, and Master of Dunster House at Harvard.

Roger Gilbert, director and chairman of the executive committee of Panhandle Producing and Refining Company, has been elected president, succeeding John V. Boyce, who has tendered his resignation.

Homer H. Haggard, formerly a member of the Hercules Powder Company research staff, has joined the Export Department to assist in the development of South American activities. He became associated with Hercules in 1946 as a research chemist in the Experiment Station, the company's central research laboratories outside Wilmington.

John I. Hardy, animal fiber technologist for the USDA, has retired after serving the Bureau of Animal Industry for 28 years. Dr. Hardy plans to operate a laboratory at Lemont, near State College, Pa.

Henry Townley Heald, president of the Illinois Institute of Technology in Chicago, has been selected as chancellor of New York University. In 1938, Dr. Heald was named president of Armour Institute of Technology. He became president of Illinois Institute of Technology in 1940, when Armour Institute was combined with Lewis Institute in Chicago to form the new institution. In addition, he is president of Armour Research Foundation of the Illinois Institute.

Robert Willis Hellwarth, a senior in electrical engineering at Princeton, has won the Albert G. Milbank prize as Princeton's ranking scholar.

Harold E. Himwich, chief, Clinical Research Division, Chemical Corps Medical Laboratories, Army Chemical Center, Md., has been appointed director of the Research Division of the Galesburg State Research Hospital at Galesburg, Ill. This hospital is devoted to the care and treatment of mental patients who are residents of the state of Illinois, and to the

study of mental disease. The program will include investigations of the functional pathology and physiology of the brain.

Herbert Hoover has been awarded the Howard Coonley Medal for long and outstanding service in advancing the national economy through voluntary standards. The American Standards Association makes the award annually. Formal presentation of the medal was made on Oct. 24 at the closing session of the National Standardization Conference in New York.

Joseph A. Jackobs has been named assistant professor of agronomy in the Illinois College of Agriculture. Formerly with the irrigation experiment station of Washington State College, he will take over the pasture work of the late R. F. Fuelleman.

Andre L. Jorissen has been made head of the Department of Hydraulics in the School of Civil Engineering at Cornell University. Marvin Bogema has been acting in that position since the retirement of Ernest W. Schoder in 1947. For the past two years Professor Jorissen has been in charge of the hydraulic laboratory at Pennsylvania State College and has taught fluid mechanics and related subjects.

Howard H. Kendler has been appointed chairman of the Department of Psychology at New York University's College of Arts and Science. Dr. Kendler was recently promoted from an associate professorship to full professorship of psychology.

Donald F. Kita has joined the Biochemical Research and Production Division of Chas. Pfizer & Co., Inc.

Paul E. Klopsteg, professor of applied science and director of research of the Northwestern Institute of Technology, has been appointed assistant director of the National Science Foundation for the Division of Physical, Mathematical, and Engineering Sciences. Dr. Klopsteg will begin his new duties with the foundation on Nov. 1, having been granted leave of absence from Northwestern. He will continue to serve the AAAS as a member of the Executive Committee.

Hans Ludvig Kottmeier, chief physician of the Radium Home in Stockholm, will lecture for three months at the obstetric-gynecological department of Vanderbilt University. He is the third Swedish physician to be invited to this university. The Radium Home in Stockholm was founded in 1910 and specializes in radiological treatment of cancer.

Nils Lofgren, on a year's leave of absence from the University of Stockholm, has been appointed an instructor in chemistry of the University of Tennessee Medical Units in Memphis.

The Senate Labor and Public Welfare Committee has indorsed President Truman's nominations of George W. Merck, board chairman of Merck & Co., Inc., and Earl P. Stevenson, of Arthur D. Little, Inc., to be members of the governing board of the National Science Foundation. The former will fill the unexpired

term, ending in May 1954, of Edward L. Moreland, deceased. The other vacancy resulted from resignation of Charles E. Wilson, whose duties as defense mobilizer prevent his service on the NSF board.

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The Johnson & Johnson Research Foundation, New Brunswick, N. J., has appointed Osgood D. Priddle, Jr., as senior pharmacologist. Dr. Priddle has taught at Purdue and at Loyola University, and has worked for the Wilson Laboratories and Professional Research Associates, Chicago.

The American Schools and Colleges Association has named Frank C. Russell national chairman of the Horatio Alger Awards Committee. Mr. Russell received a 1951 Alger Award for outstanding achievement accomplished through industry and ability despite humble origin.

Tracy M. Sonneborn, of Indiana University, returned recently from Chile, where he gave a series of ten lectures in the Department of Biology, University of Chile's School of Medicine, in Santiago, on the genetics of microorganisms. He also lectured before the Society of Biology of Santiago, the medical faculty of the university, and the biology societies of Valparaiso and Concepción.

Ernest S. Tierkel, of Atlanta, veterinarian in charge of rabies control activities for the Communicable Disease Center, is on a three months' tour of duty in Europe, Africa, and Asia under the auspices of WHO. Making his base at the Geneva WHO headquarters, he will first be assigned to Northern and Southern Rhodesia. Next, working out of Alexandria, he will assist India and Pakistan and several countries of the eastern Mediterranean region, including Iraq, Lebanon, Syria, Jordan, and Israel.

Education

Aligarh University and the University of Jammu & Kashmir have jointly set up a research observatory at Gulmarg (geomagnetic latitude 23° 32′ N at longitude 75° E) for cosmic-ray work. Situated at a height of 9,000 feet, 28 miles from Srinagar, capital of the state of Jammu & Kashmir, the observatory can remain open only from Mar. 15 to Oct. 31. Power at present available is 220 a-c at 25 cycles, but the government may supply 220 a-c at 60 cycles within the next few years. P. S. Gill, Aligarh professor of physics and dean of the Faculty of Science, has been made honorary professor of physics at Jammu & Kashmir, and has been appointed observatory director.

New appointments to the full-time faculty of the Hahnemann Medical College include James B. Donaldson, Harry Goldberg, Catherine Lewis, Daniel J. Marino, D. Peter Oesper, W. Robert Penman, John W. Van Dyke, Arthur Wase, and Russell W. Weller.

The Edward K. Dunham Lectureship, established in 1923 at Harvard, will be held this year by E. B. Verney, professor of pharmacology, University of Cambridge. Lectures will be given on Oct. 31, Nov. 1, and Nov. 6.

Indiana University has added the following to the Physics Department staff: Keith A. Brueckner, of the Institute for Advanced Study; Kenneth M. Watson, of the UC Radiation Laboratory; Volney K. Rasmussen; and Dan W. Miller. Kai Siegbahn, of the Nobel Institut, and J. Mattauch, of the Max Planck Institut für Chemie, were recent guest lecturers in the department.

The University of Michigan Expedition to the Near East, financed by the Carnegie Corporation, the Rockefeller Foundation, the Wenner-Gren Foundation, and the Rackham School of Graduate Studies, has brought back an exact rubber copy of an inscription carved in the stone walls of a 10,000 foot pass between Iran and Iraq. Although known for years, the inscription has never been copied, and it is hoped that study will result in finding the key to hitherto unknown languages. The expedition also made a survey of the Kurdish city of Rowanduz, each member studying his specialty. Michigan staff members were Douglas D. Crary and M. Marbury Efimenco. Ralph Solecki, Smithsonian Institution archaeologist, also was with the group.

Chikatoro Togari, dean of Nagoya University, Tatsuo Ozawa, of the medical bureau of the welfare ministry in Tokyo, and Yukio Yoshida, assistant chief of Japanese medical affairs, are in this country on a three-month U. S. Army-sponsored tour to gather ideas and information that will be useful in rebuilding Japanese hospitals and medical schools. Dr. Togari is studying American teaching methods, and Dr. Yoshida and Mr. Ozawa are interested primarily in hospital administration.

The National Association of Biology Teachers, assisted by a grant-in-aid from the American Nature Association, has begun a three-year project aimed at emphasizing conservation teaching in biology programs. State chairmen and committees are particularly interested in how various teaching techniques have been used to increase interest in conservation, such as field trips, films, camps, school forests, nature trails, use of community resources and agencies, group work, schoolground projects, fairs, exhibits, and the like. Local, state, regional, and national workshops are planned to permit biology teachers and others to develop adequate criteria for good teaching, to share experiences, organize descriptive material submitted by teachers, and to assist in developing projects and programs in schools interested in initiating a stronger conservation program. The first regional workshop is planned for Philadelphia Dec. 28 and will be held in the Hotel Adelphia as a part of the annual meeting of the NABT. A national committee, consisting of the state and regional chairmen, and an executive committee of seven will guide the project and will be assisted by an Advisory Committee of representatives of 25 national conservation groups. Anyone willing to assist in the project in any way is requested to write to Richard L. Weaver, Project Leader, P. O. Box 5424, State College Station, Raleigh, N. C.

In an educational program sponsored by New

Mexico A & M College, 39 agricultural extension workers from 13 Latin-American countries spent more than two weeks on the A & M campus for orientation, then six weeks in rural New Mexico, working with county extension workers. On Oct. 8 they took a special bus to Washington, D. C., visiting Oklahoma A & M, the universities of Arkansas and Tennessee, the TVA, and Virginia Polytechnic Institute. After their week in Washington, they returned to their home countries. The institute is the first Point 4 project under which an American college has undertaken to give resident training to a large non-English-speaking group in the principles and practices of agricultural extension.

The second Harvey Lecture of the current series at the New York Academy of Medicine was given by Frank R. Winton, of University College, London, on Oct. 25. Other speakers will be: Horace W. Magoun, Nov. 15; W. Barry Wood, Jr., Dec. 20; I. L. Chaikoff, Jan. 17; Carroll M. Williams, Feb. 21; Louis B. Flexner, Mar. 20; Walter H. Seegers, Apr. 17; and L. Zechmeister, May 15.

Grants and Fellowships

Alpha Xi Delta Fraternity has awarded a fellowship to Eloise M. Lemon, fellow in oncology at the Woman's Medical College of Pennsylvania, for the continuation of her study of home care of indigent cancer patients. The American Federation of Soroptimist Clubs will support the work of Phiroza Davar, of Bombay, fellow in anatomy. Dr. Davar hopes to use part of the award to finance six mouths of research in public health fields in the U. S. before she returns to India next year.

The Atomic Energy Commission offers eight fellowships in industrial medicine for 1952–53. Awards are for one year's academic training at approved institutions, after which fellows will be eligible to apply for a second year's in-plant training at one of the major AEC installations. Stipend for the first year will be \$3,600, plus tuition and laboratory fees, and for the second, \$5,000. The University of Rochester administers the program. Applications should be submitted by Jan. 1 to H. A. Blair, A. E. Fellowships in Industrial Medicine, Atomic Energy Project, University of Rochester, School of Medicine and Dentistry, Rochester, N. Y.

A Food Processing Fellowship has been established at Illinois Institute of Technology as a tribute to Harry McCormack, for 38 years director of the Department of Chemical Engineering and technical consultant to Putman Publishing Company, publishers of Food Processing magazine. Daniel J. Heald, of Lowell, Mass., has been selected as the first fellow.

The A. L. Harris Company, of Dallas, through the Southwestern Medical Foundation, has awarded a prize of \$1,000 to Charles M. Pomerat, professor of cytology and director of the University of Texas Tissue Culture Laboratory, Galveston, for his contribution to scientific knowledge of cell growth. Dr. Pomerat has been professor of cytology at Texas U since 1943.

The Office of Naval Research and the Flight Research Laboratory expect to make funds available for a few small contracts to support individual research in theoretical mathematics, intended primarily for postdoctoral students. Evaluation of proposals will be made in consultation with an advisory committee appointed by the National Research Council. Applications must be submitted before Jan. 2 on forms that may be obtained from Chas. R. DePrima, Mathematics Branch, ONR, Washington 25, D. C.

In the Laboratories

Armour Research Foundation has sent S. W. Schwartzman, biochemist and microbiologist, to Jamaica to head a new leather project sponsored by the Harty Leather Company, Kingston. Technological improvements in production, standardization of the firm's operations, and investigation of possible uses of tannery by-products are objects of the research.

Kanthal Corporation, an American subsidiary of the Kanthal Company, of Hallstahammar, Sweden, has recently been established at Stamford, Conn. The factory will produce alloys according to the patents and methods of the parent company and will take over the distribution of Kanthal products in the U. S., previously handled by C. O. Jelliff Manufacturing Corporation.

American Cyanamid Company has added the following scientists to its Lederle Laboratories Division at Pearl River, N. Y.: Mary-Anne Angell, biologist; Raymond A. Brown, Norbert E. Harrington, and Milton D. Heller, chemists; Donald C. Reihard, bacteriologist; and C. Richard Walter, sanitary engineer.

The Charles R. Robertson Lignite Research Laboratory of the Bureau of Mines was formally dedicated and opened at Grand Forks, N. D., Sept. 29. Secretary of the Interior Oscar L. Chapman and James Boyd, whose resignation as director of the Bureau of Mines has just been announced, officiated. The laboratory is named after the late Congressman Charles R. Robertson, whose efforts led to the building of the \$750,000 structure, which will provide modern facilities for the cooperative program of the University of North Dakota and the Bureau.

Reserve Mining Company, owned by Republic Steel Corporation, the Armeo Steel Corporation, and National Steel Corporation, has awarded contracts for the construction of a \$75,000,000 beneficiation plant at Beaver Bay, Minn., first U. S. taconite production facility. An Eric Mining Company plant at Aurora, Minn., although still in the pilot stage, is expected to be on a production basis soon. If the projects are successful they will considerably extend the nation's iron ore reserves.

Western Cartridge Company has added three new members to its Explosives Department: Robert A. Cooley, as head of a new group to study rocket powder easting; John N. Mandas, Rocket Propellants Group; and Howard L. Wolsted, Dynamite Group.

Meetings and Elections

The Fiftieth Anniversary Meetings of the American Anthropological Association will be held at the Palmer House, Chicago, Nov. 15-17. Special meetings of the Central States Branch, AAA, the American Association of Physical Anthropologists, the Society for American Archaeology, and the Society for Applied Anthropology will be held at the same time. Main interest will center in the three symposia on "The Training of the Professional Anthropology," and "The Scope of Modern Physical Anthropology," and "The Positive Contributions of Social Anthropology."

Duke University Medical School's Annual Symposium has been replaced this year by a new medical lecture series, cosponsored by the North Carolina Academy of General Practice. Three one-day meetings, during the period Oct. 13–Nov. 10 will offer addresses on mental deficiencies, abnormal heart and lung conditions, and medical effects of the A-bomb. The first lecturers were Clemens A. Benda and Woodard D. Beacham. Future speakers will be A. McGee Harvey, Herman E. Pearse, Isaac A. Bigger, and Tinsley Harrison.

Newly elected officers of the Mount Descrt Island Biological Laboratory are Homer W. Smith, president; E. K. Marshall, Jr., vice president; Charles E. Wilde, Jr., secretary; Albert Cunningham, treasurer; and Warner F. Sheldon, director.

A Scientific Congress was held in Mexico City Sept. 24-30 under the auspices of the National Independent University of Mexico at the celebration of the 400th aniversary of its founding. More than 1,500 papers and reports were presented in the five sections. U. S. guests participating in the medical program included K. F. Meyer, Henry Helmholtz, E. S. Guzman Barron, Lewis N. Katz, and Chauncey D. Leake. The Division of Biological Sciences and Medicine was under the direction of Ignacio Gonzales Guzmán.

The first Symposium on the Physics and Medicine of the Upper Atmosphere, jointly sponsored by the Air Force School of Aviation Medicine and the Lovelace Foundation for Medical Education and Research, of Albuquerque, N. M., will open Nov. 6 in San Antonio. Authorities in aeronautical design, astrophysics, radiobiology, and medicine will be heard, with discussions focused on the aeropause. In addition to the formal papers, there will be round-table conferences on the symposium subject, on "Vehicles for Physical and Biologic Research in the High Atmosphere," and on "Problems of Human Travel at Increasing Altitudes." Attendance is by invitation only, but the proceedings will be made public and no secret information will be discussed. The material will later be published in book form by the University of New Mexico Press.

The Uruguayan Association for the Advancement of Science has elected Rodolfo V. Talice president, Clemente Estable vice president, Oscar J. Maggiolo-Campos secretary, and José L. Duomarco treasurer.

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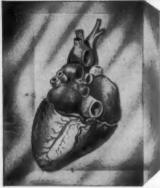
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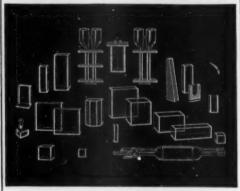


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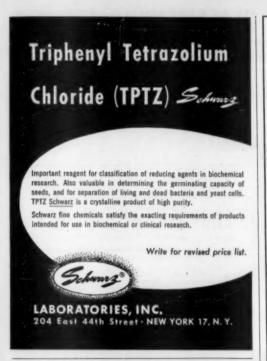
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